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PARAMYOTONIA CONGENITA*

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MYOTONIA is one of the most interesting of common neurological signs. It is characterized by delayed relaxation of affected muscle bellies which have been contracted voluntarily or by means of electrical or mechanical stimuli. Although any striated muscle may show myotonic responses, the phenomenon is usually best demonstrated in the tongue and thenar eminences. The pathogenesis and full significance of myotonia remain incompletely understood despite recent studies of biochemical, electromyographic and pathological changes in the affected muscles.

Clinically, myotonia is a prominent sign in three of the inherited primary disorders of muscle, myotonia congenita (Thomsen's disease), dystrophia myotonica and paramyotonia congenita.

In Thomsen's disease the myotonic disorder is widespread and is often associated with marked muscular hypertrophy. The disorder is first manifested in infancy or childhood, and affected individuals may have great difficulty initiating voluntary movements of their limbs. Percussion and active myotonia are demonstrable in almost all striated muscle groups. A proportion of these patients will develop signs of dystrophia myotonica later in life.

Dystrophia myotonica is the best known syndrome in which myotonia is a prominent sign. The disorder usually first appears in middle age and is slowly progressive thereafter. Percussion myotonia is often confined to the tongue and thenar eminences; and active myotonia is most apparent in the hand grips. These patients exhibit dystrophic symptoms manifested by bilateral facial weakness, weak and wasted sternomastoid muscles and atrophy of muscles of the forearms, hands, legs and feet. Frontal baldness, cataracts and endocrine abnormalities are common associated findings.

Paramyotonia congenita is a familial disorder first described by Eulenberg[1] in 1886. The precipitation of active myotonia by exposure to cold temperatures and the liability to prolonged attacks of muscle weakness and stiffness in the extremities constitute its most distinguishing clinical features. This syndrome is very much rarer than either myotonia congenita or dystrophia myotonica. Only three affected kinships have previously been described in this hemisphere.[4] We wish to report the clinical features of a Canadian family with paramyotonia congenita.

CASE HISTORY

Peggy C., a 13-year-old girl, was referred for neurological assessment in February 1959, because of two episodes of weakness in her lower extremities. Her mother, who is an excellent observer, gave the following history.

Peggy had been known to show unusual reactions to cold since infancy. If the mother left her to sleep in a room with the window open on a cold day, she would return to find the child's face peculiarly contorted. Her eyes would be closed, the corners of her mouth retracted and the facial skin wrinkled. Should the child sneeze when her face was cold, the expression of the sneeze would freeze on her face. If her hands had been under the blanket they would be normal, but if they had been outside and were cold, the fists would be clenched and she seemed unable to open them. All of these signs would gradually lessen and disappear as the child became warm.

Peggy herself first became aware of these unusual reactions to cold when she started attending school. She found that walking against a cold wind would cause her face to feel stiff and tight and that if her hands became cold they would curl up into a fist. She took particular care to protect her face and hands well when out of doors and learned that these symptoms were less likely to occur if she kept very active. Neither she nor her family regarded these symptoms as important, and medical aid was not sought because of them.

The first episodes of weakness in the lower extremities occurred in the spring of 1958. She had gone to church that morning, having eaten a very small breakfast. When she attempted to stand during the service she found that her knees felt weak and her legs would not hold her. There were no associated pains or paresthesias. Later her mother helped her to her feet and she improved considerably after walking with assistance. During this period she "placed her feet as though not sure they would hold her". Her legs continued to feel weak and unsure until after she had eaten her dinner.

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Fig. 1.—Percussion myotonia of the tongue of patient's father.

The second episode of weakness developed on Valentine's Day in 1959. The day had been relatively mild, and Peggy had worn a skirt to school, rather than the slacks she usually wore in the winter. She noted that her legs felt chilly and about 11.30 a.m. commented that her thigh muscles felt stiff. Later in the day she experienced difficulty standing up by her desk because of a weak sensation in her knees. At 3.30 p.m. she was able to walk the two blocks to her home only with difficulty. Her mother characterizes the patient's gait at that time by saying that "she was lifting her feet too high in the air and stamping them down." On returning home Peggy was put to bed and her legs were warmed. By 10 p.m. that evening she was able to walk normally and the feeling of stiffness had disappeared.

The patient's father and her two younger sisters show similar reactions to cold. The father, who was 37 years old, had been aware of similar symptoms referable to his face and hands since childhood. His symptoms had become less troublesome in adult life and he had never sought medical advice regarding them. Similar symptoms on exposure to cold had been noted in the two younger children in infancy. Peggy is the only member of the family who has experienced episodes of leg weakness.

On examination Peggy was found to be a pleasant, healthy appearing girl of average intelligence. Dystrophic signs were carefully sought and none could be demonstrated. In particular, she smiled readily, retracted the corners of her mouth well, could whistle, and could bury her eyelids completely. The sternomastoid and trapezius muscles were of normal bulk and strength. No muscle weakness, atrophy or fasciculations could be demonstrated in the extremities or about the shoulder or pelvic girdles. Her gait was normal and she had no difficulty standing or hopping on either foot unaided. Definite percussion myotonia of the tongue could be demonstrated at room temperature. No active myotonia was apparent in her hand grip, and percussion myotonia of the thenar eminences could not be demonstrated. However, percussion of the extensor muscles of the forearm resulted in a dorsiflexion movement of the wrist which was sustained slightly longer than in a control subject of the same age. There were no other apparent abnormalities of muscle tone. Deep tendon and superficial reflexes were active and symmetrical. Plantar responses were flexor. No cerebellar incoordination or sensory deficit could be demonstrated.

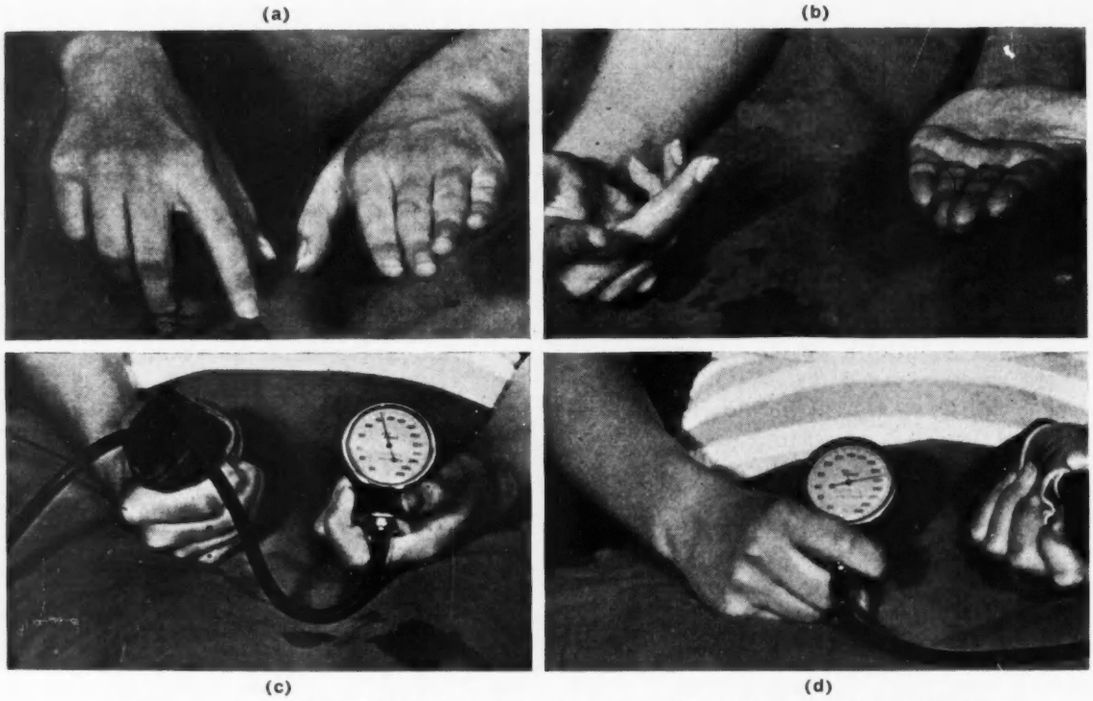

Fig. 2 a, b, c and d.—Patient's hands after immersion of right hand and forearm in water at 60° F. for 12 minutes. (a) Appearance of hands immediately after removal from water. (b) Attempted extension of fingers after both hands have been voluntarily clenched once. (c) Muscle weakness demonstrated in the right hand. (d) Uncooled hand showing normal power.

Complete neurological examinations were also carried out on Peggy's father and his other two children. They showed findings which were exactly similar to Peggy's, i.e. constant percussion myotonia of the tongue (Fig. 1), doubtful percussion myotonia of the forearm muscles, no active myotonia and no dystrophic features. The absence of dystrophic signs in the father must be emphasized. Peggy's paternal grandparents were also examined by one of us (P.D.). Neither showed any dystrophic signs or myotonic

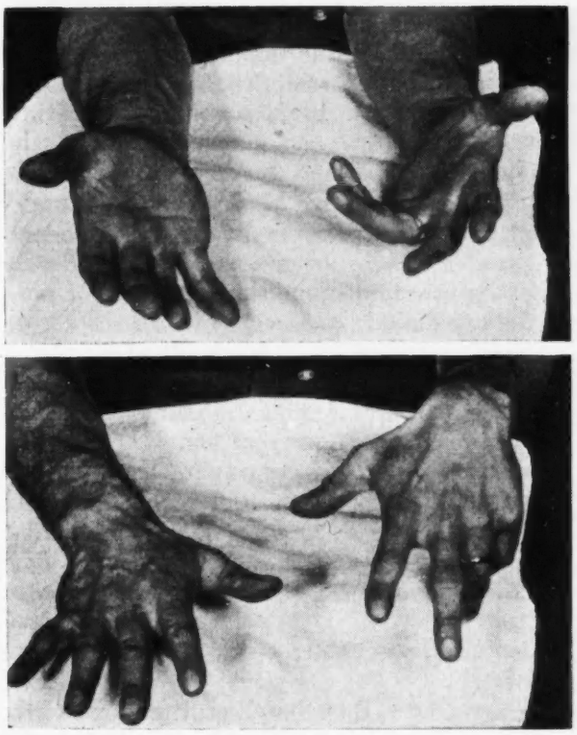

Fig. 3 a and b.—Father's hand after immersion of the left hand and forearm in water at 60° F. for 15 minutes.

phenomena. They had been aware of the unusual reaction of their son to cold since he was three or four years of age. They denied knowledge of any other member of their family with symptoms suggestive of a myotonic and/or dystrophic syndrome.

Further observations were made regarding the effects of cold on the extremities of these patients. Under normal temperature conditions, Peggy could move a sphygmomanometer dial to 220 by squeezing a semi-inflated cuff with her right hand. We then immersed her right hand and forearm in a water bath at 60° F. After twelve minutes the limb was removed and dried. It was then found that the patient was unable to maintain extension at the metacarpophalangeal joints and that the fourth and fifth fingers were tonically flexed (Fig. 2a). Individual finger movements were grossly impaired. Flexion and extension finger movements were still possible, but neither the fourth nor the fifth fingers could be fully extended. Repeated opening and closing movements of the hand increased the tendency to finger flexion and further impaired her ability to extend the fourth and fifth fingers (Fig. 2b). Her hand grip was considerably weakened as evidenced by her ability to move the sphygmomanometer dial only to 90 (Fig. 2c). Her finger flexors were also weak. There was slight weakness of wrist extension. No percussion myotonia of the thenar eminence could be demonstrated and the suggestion of percussion myotonia in the extensor forearm muscles was no longer present; in fact, there was not even a normal reaction to percussion of the muscle groups which had been cooled. The father's hand showed the same abnormalities after exposure to cold for a similar period (Fig. 3 a, b).

Peggy's hand and forearm were then re-immersed in water at 60° F. for a further 10 minutes. At the end of this period all of the fingers and the thumb were tonically flexed. Voluntary extension of the fingers and thumb at the metacarpophalangeal joints was impossible (Fig. 4a). These digits could be easily extended passively but slowly returned to their flexed position as soon as the passive force was withdrawn. Further voluntary finger flexion was possible, but when the fist was clenched this posture was maintained and the fingers could not be returned to their original position (Fig. 4b). When the manometer bulb was placed within the tonically flexed fingers, the patient could move the dial only to 40 (Fig. 4c). When the arm was held outstretched there was partial flexion of the right wrist, and voluntary extension of the wrist could be easily overcome. Wrist flexion was weak, but much less so than wrist extension. Direct percussion of the forearm and thenar muscles failed to excite either a normal reaction or a myotonic response. The muscle bellies of the forearm and hand seemed firmer than normal on palpation. The three other affected members of the family were observed under these same conditions and showed exactly similar reactions.

Immediately following these observations Peggy was immersed from the neck down in a Hubbard tank containing water at 68° F. for 25 minutes. At the end of this time the fingers of both hands were held in a semi-flexed position, voluntary movements of the fingers were grossly reduced, and weakness of the small hand muscles, finger extensors, finger flexors and wrist extensors could be demonstrated. The muscles of the

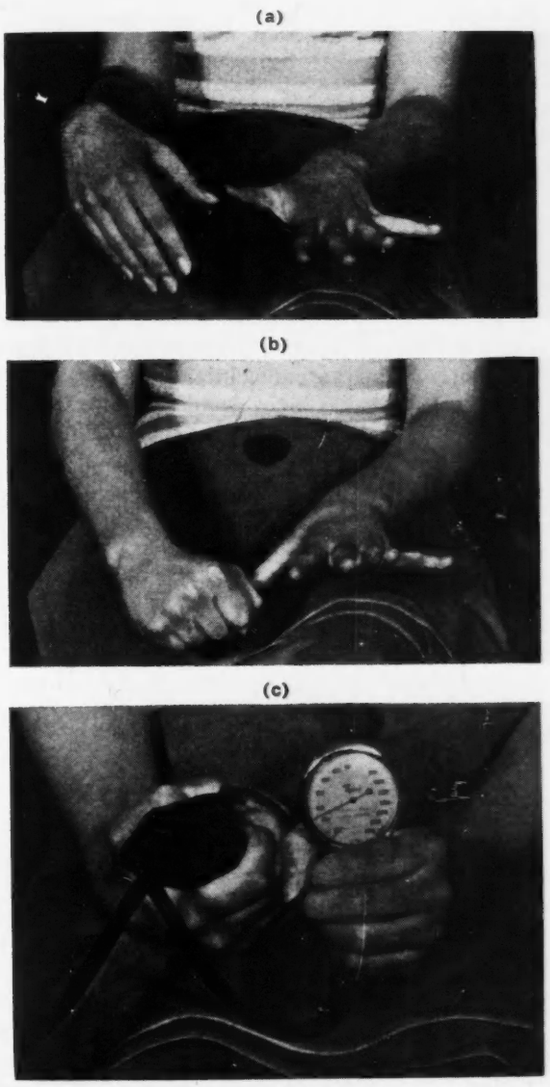

Fig. 4 a, b, and c.—Patient's hands after re-immersion in water at 60° F. for further 10 minutes.

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right hand and forearm had not returned to normal prior to this total immersion and they remained much weaker than the more recently cooled muscles of the left hand and forearm. The patient shivered violently when removed from the Hubbard tank. Diffuse but mild generalized muscle weakness was apparent in both lower extremities. Percussion myotonia could not be elicited in any site other than the tongue.

An attempt was also made to demonstrate the effect of cold on Peggy's facial muscles. We applied an ice bag to one side of her face but this was very uncomfortable and could be tolerated for only three minutes. At the end of this time the only effect noted was a narrowing of the palpebral fissure on the cooled side (Fig. 5).

Fig. 5.—Patient's face after an ice bag had been applied to the left side for 3 minutes.

Routine hematological studies, urinalysis, and fasting and two-hour postprandial blood sugar levels were normal. Her serum electrolyte values showed a sodium level of 140 mEq./l., potassium 5.4 mEq./l., and chlorides 106 mEq./l. A second spot serum potassium determination was 4.6 mEq./l. Serum potassium estimations were also made from venous blood drawn simultaneously from the antecubital fossa of the right and left arms after the right hand and forearm had been immersed in water at 60° F. for 20 minutes. The blood from the left arm contained 4.5 mEq./l. of potassium and that from the right 4.35 mEq./l.

An electromyogram was recorded (by Dr. T. Hunt) with the electrodes placed in the extensor communis muscle both before and after cooling the forearm. A definite increase in insertion potentials, characteristic of myotonia, was easily demonstrated at room temperature. After cooling the extremity, a similar increase in insertion potentials could be demonstrated but no action potentials were recorded on attempted voluntary contraction.

DISCUSSION

Much that has been written about paramyotonia congenita concerns its relationship to Thomsen's disease. Eulenberg[1] recognized that "to a certain degree, this disease [paramyotonia] seems to be related to Thomsen's disease" but felt that there were sufficient clinical and electrophysiological differences to justify a separate classification. In agreeing with the foregoing observation, Bell[2] comments that "the effect of cold on myotonia from any source is often very marked, but that the condition should only manifest itself under conditions of cold certainly places the condition in a different category from that characteristic of Thomsen's disease." Thomasen,[3] in 1948, concluded that there were sufficient clinical and genetic differences between paramyotonia and myotonia congenita to justify their distinction. More recently, Drager, Hammil and Shy[4] have emphasized the mode of inheritance and the occurrence of episodes of flaccid paralysis as distinguishing features of paramyotonia congenita.

The opposing view, that paramyotonia is merely a clinical variant of myotonia congenita, has been held by the majority of clinical investigators. There are numerous case reports of families in which some members suffered from paramyotonia congenita while others had typical myotonia congenita. Paramyotonia has also been described in families with dystrophia myotonica—and occasional patients with paramyotonia who also had dystrophic signs have been reported. This point of view is well presented and documented in two papers by Maas and Paterson.[5, 6]

Our own view is that the clinical features of the paramyotonic syndrome are so characteristic as to deserve a distinctive classification. This is not to deny the close association of paramyotonia with myotonia congenita and dystrophia myotonica. Rather, we would visualize each of the three primary myotonic syndromes as usually running true to form, and with a distinctive form of inheritance, in any given family. The appearance in some families of members with myotonic, paramyotonic and dystrophic features emphasizes the fundamental unity of all three syndromes and supports the adage that inherited disorders should be looked upon as "families and not diseases".

The importance of the paramyotonic syndrome lies not in its classification, but in the relationship which its symptomatology suggests between the myotonic syndromes and the syndromes of familial episodic flaccid paralysis such as periodic paralysis and adynamia episodica hereditaria.[7] In this connection it is worth while looking more closely at the motor disability in the hands of our patients before, during and after cooling. Prior to cooling we were unable to demonstrate any motor deficit other than minimal percussion myotonia in the extensor muscles of the forearm. A more definite percussion myotonia appeared *transiently* in the wrist extensors and thenar muscles during the early phase of cooling. However, by the time active myotonia and muscle weakness were evident, percussion myotonia could no longer be evoked. Most investigators have accepted the weakness and abnormal positioning of the hands of these patients as due to the development of active myotonia in the small hand muscles. But there are some unusual features of this motor deficit. First, and probably least important, is the worsening of the active myotonia by repeated flexion movement of the fingers. This myotonia paradoxica is commonly seen in para-

myotonia and may be seen occasionally in otherwise typical cases of myotonia congenita or dystrophia myotonica. Secondly, it is questionable whether all of the weakness which develops is truly due to the development of myotonia. A muscle showing active myotonia is unresponsive to faradic or galvanic stimulation and cannot be voluntarily or artificially contracted by motor stimulation. The muscle is in fact paralyzed although contracted. This state of affairs presumably existed in the cooled small hand muscles and finger flexors of our paramyotonic patients. But can a myotonic paralysis of muscle account for the marked weakness of wrist extension which these patients developed? One might argue that the apparent weakness of wrist extension was due to the development of myotonic contraction in both wrist flexors and extensors, but more marked in the former. We doubt that this is the case, since the wrist could be easily extended passively, and paralysis of wrist extension was almost complete at a time when voluntary flexion of the wrist was still strong. Further, we could not demonstrate either active or percussion myotonia in the wrist extensors at this stage. It appeared rather that the wrist extensors were in a state of flaccid paralysis in contrast to the state of myotonic paralysis of the small hand muscles. Thirdly, the functional deficits in the cooled hands of paramyotonic patients is unusual in that the weakness of both small hand muscles and wrist extensors lasts for hours after rewarming has occurred, and the weakness persists longer than active myotonia can be demonstrated.

Drager, Hamill and Shy[4] rightly lay great stress on the episodes of proximal limb weakness to which paramyotonic patients are liable. They describe a family with paramyotonia in which some members were liable to episodic attacks of flaccid paralysis of proximal musculature. In one patient these attacks were of such severity that he was unable to lift his head from the bed and had to be turned by others. A younger member of the same family developed "flaccid paralysis of the extensors of the wrists and fingers" after whole-body immersion for 20 to 30 minutes in water at 68° F. On reviewing the literature it is evident that the episodic limb girdle weakness experienced by many paramyotonic patients is less dramatic and severe than that in Drager's family. For example, Eulenberg in his original description of paramyotonia describes a state of "Klammheit" which "will occur in the lower extremities when he is sitting or in bed with inadequate clothing." He defined "Klammheit" as spasms of rigidity brought on by cold, disappearing quickly in some muscles, but persisting in others like a paralysis. In describing a second patient he comments that "on trying to get up he almost fell, and he had considerable stiffness while sitting. Flexion and extension at the knees and movements of the foot were particularly slowed down." If we look again at the two episodes of leg weakness which our patient Peggy experienced, we find that both were preceded by periods of immobility and exposure of the legs to moderately cool temperatures. Although a sense of "stiffness" in the thigh muscles was described, it seems clear that the major disability was due to weakness and not muscle stiffness. It would appear therefore that prolonged exposure to cold, particularly if associated with periods of immobility and fasting, renders paramyotonic patients liable to prolonged episodes of limb weakness which may be either myotonic or flaccid in type.

Clinically, paramyotonia and familial periodic paralysis have many features in common. Both syndromes make their appearance early in life and symptoms tend to be less severe after middle age. In neither condition do dystrophic features commonly occur, although they may occasionally appear in either. In both syndromes attacks of generalized or local paralysis may be evoked by exposure to cold. Patients with periodic paralysis commonly give a history of attacks appearing in the morning after sleeping in a cool room. Such attacks may or may not be associated with hypokalemia. Local weakness in an extremity may be provoked in some patients with periodic paralysis by exposing the extremity to cold.[8, 9] Further, although the weakness of periodic paralysis is commonly described as flaccid, it has been noted that "the muscles had a firmness to touch quite different from that of a denervated limb."[8] The same is true of the paralyzed muscles of a paramyotonic patient. In both disorders, recovery from attacks of muscle weakness occurs gradually over a period of several hours.

The precise pathogenesis of myotonic phenomena and periodic paralyses is not known. It is possible that the fundamental abnormality in both conditions lies in the muscle membrane. The integrity of this membrane appears essential for the regulation of intracellular/extracellular K+ and Na+ gradients during muscle rest and activity. These gradients must be maintained for the normal reception of motor impulses, the conduction of the muscle potential from the neuromuscular junction to the remainder of the fibre, and the activation of the contractile elements in the fibre.[10] Myotonic muscles are known to be unusually sensitive to K+, and the K+ content of myotonic muscles may be less than normal.[11] On the basis of this and physiological evidence[12] it is assumed that an abnormality of the muscle membrane is fundamental to the myotonic state. In periodic paralysis, the abnormalities of muscle membrane function have often been considered secondary to abnormal electrolyte states, particularly hypokalemia. However, many patients have now been described who experience typical attacks of periodic paralysis with normal or high levels of serum K+. It has also been emphasized that even in hypokalemic periodic paralysis the muscle weakness usually appears with levels of serum K+ higher than that which will cause weakness in a normal individual. These facts have led several observers to suggest that, as in

myotonia, the basic disorder of function in periodic paralysis may lie in the muscle membrane.[8, 9] Further support of this concept comes from the recent report of a family whose members experience periodic attacks of hyperkalemic periodic paralysis and who also show myotonic phenomena.[13]

SUMMARY

A family whose members show symptoms and signs of paramyotonia congenita is described. The importance which this syndrome bears in relation to the other myotonic syndromes and to the familial periodic paralyses is discussed.

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PREGNANCY IN THE ABSENCE OF ADRENAL CORTICAL FUNCTION*

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FUNCTION OF the adrenal cortex is lost in Addison's disease and after surgical bilateral total adrenalectomy in the treatment of Cushing's syndrome due to hyperplasia of the adrenal cortex, and for bilateral tumours of the cortex or medulla. After unilateral adrenalectomy for a single tumour or after subtotal adrenalectomy, adrenal insufficiency may occur in some cases. The advent of potent adrenal steroids has made the management of patients with adrenal insufficiency relatively easy and has remarkably improved the prognosis of these patients. Although the number of patients with these conditions is relatively small, there have been an increasing number of reports of pregnancy in patients who have adrenal cortical insufficiency and are receiving adequate substitution therapy.

The prognosis in untreated Addison's disease is said to be extremely poor. Brent[2] reported 39 cases and added one, a patient who died after a Cesarean section. Knowlton, Mudge and Jailer[9] recorded 39 pregnancies in 29 patients with Addison's disease prior to 1950. In eight out of 12 (67%) well-documented cases, the patients died during or soon after the termination of the pregnancy. These authors added five cases of their own. Hendon and Melick,[5] in a review of the literature, recorded 60 cases of pregnancy in Addison's disease; 14 of the pregnancies occurred after potent replacement therapy was available. There was one maternal death in the latter group. To this number they added one successfully managed case of their own. Allahbadia[1] reported one successful pregnancy in a patient with Addison's disease, despite the fact that the patient developed mild toxemia and required induction of labour. Moore, Freedman and Green[13] and Kaiser[7] each reported a patient with Addison's disease who was followed through a successful pregnancy. Single cases have been reported by McFarlane and Truelove,[12] Singh[17] and Kirk.[8] The first of these resulted in the neonatal death of a premature infant; in the latter two, the infants survived. Hunt and McConahey[6] reported one case of pregnancy managed successfully in a patient with Addison's disease who was treated by adequate substitution therapy, and two pregnancies successfully concluded in two patients who developed Addison's disease post partum. Rolland, Matthews and Matthew[15] reported two patients with Addison's disease who were successfully managed through pregnancy although one of the patients died six months after delivery in addisonian crisis precipitated by an attack of influenza.

The prognosis in untreated Cushing's syndrome is poor although it is somewhat better than in untreated Addison's disease. Plotz, Knowlton and Ragan[14] reported that 17 of 32 patients (53%) with Cushing's syndrome were dead within an average of five years from the time of onset of their symptoms if the condition was untreated. With modern adrenal steroid substitution therapy available, extended surgical procedures for Cushing's syndrome have permitted the survival of more patients with this condition, and reports of pregnancies successfully carried through in patients with previous bilateral adrenalectomy are increasing in number. Hunt and McConahey[6] have reported one case of pregnancy successfully concluded following bilateral total adrenalectomy for a pheochromocytoma involving both adrenals. Schneider, Weed and Bowers[16] reported two successful pregnancies in two patients following bilateral total adrenalectomy for Cushing's syndrome. Estrada *et al.*[3] reported one successful case as did Worner and Matthew[19] and Tivenius.[18]

Hunt and McConahey[6] reported seven pregnancies in four patients with untreated Cushing's syndrome. The fetal loss was three out of seven

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pregnancies, or 43%. It was their feeling that the chief threat to the pregnancy was the coexisting hypertension. One of these patients died from a cerebral vascular accident 20 months after delivery. Following surgical treatment of four of five patients with Cushing's syndrome and x-ray therapy to the pituitary in the remaining patient, four pregnancies out of the five were successfully terminated. One patient with adrenal cortical insufficiency after subtotal adrenalectomy aborted at 10 weeks' gestation. In two pregnancies in a patient with untreated bilateral pheochromocytoma, they reported one intrauterine death at six months and one surviving child. After bilateral total adrenalectomy this patient carried a subsequent pregnancy satisfactorily to term. In addition, Schneider, Weed and Bowers[16] reported one successful pregnancy in a patient who had undergone subtotal adrenalectomy, subsequently developed a recurrence of Cushing's syndrome, and required a bilateral total adrenalectomy. Greenblatt, Scarpa-Smith and Metts[4] reported on five pregnancies, four of which were carried to term, with one abortion among three patients with Cushing's syndrome due to unilateral adrenal cortical tumour. Of these, one had a benign tumour and two had adrenal carcinoma. One of the latter patients died one year after a second pregnancy.

It would appear therefore that an increasing number of patients with adrenal cortical insufficiency will become pregnant and will require joint management by the medical endocrinologist and the obstetrician.

CASE REPORTS

Five cases are reported below of patients with loss of adrenal cortical function who were followed through six pregnancies. One had Addison's disease and the remaining four had undergone surgical bilateral total adrenalectomy for Cushing's syndrome.

CASE 1 (Mrs. E.K.).—This 38-year-old patient was admitted to the Toronto General Hospital in June 1955 because of shortness of breath and cardiac failure. Her blood pressure was 220/140 mm. Hg. There was loss of hair on the scalp and obesity of the trunk. Her weight was 263 lb. She had had diabetes mellitus of mild degree for five years, and amenorrhea for one year. The patient had 2 plus albuminuria and a nonprotein nitrogen (NPN) value of 33 mg. %. There was evidence of lowered glucose tolerance. Content of 17-hydroxycorticosteroids in the urine was reported as 12.2 mg. in a 24-hour sample (normal 1 to 10 mg.). Her 17-ketosteroid excretion amounted to 10.9 mg. in 24 hours. There was a hyperactive response to intravenous administration of ACTH. On June 27, 1955, a total bilateral adrenalectomy was performed. The pathological diagnosis was bilateral hyperplasia; total weight of the adrenals was 32 g. The postoperative course was uneventful and the patient was stabilized on treatment with 50 mg. of hydrocortisone daily. She slowly lost the stigmata of Cushing's syndrome, but her hypertension persisted at a level of 200/100 mm. Hg when lying down. Postural hypotension was present in the erect position in which her blood pressure was 60/40 mm. Hg. The postural hypotension was eventually controlled by the use of 0.1 mg. of 9-α-fluorohydrocortisone daily. At the time of discharge on July 29, 1955, she weighed 211 lb. and was taking digitalis grains 1½ daily. On October 14, 1955, she still complained of dizziness, and postural hypotension was still evident. Her weight at this time was 178 lb. It was necessary to adjust her dosage of steroids to control the hypotension.

The patient was initially seen in the prenatal clinic on March 12, 1956. Her last menstrual period had been on November 8, 1955, and her expected date of confinement was August 15, 1956. A pregnancy of 16-18 weeks' gestation was confirmed at that time. Her blood pressure in the recumbent position was 200/100 mm. Hg; she had 2 plus albuminuria. Urine culture grew *E. coli*. The Kahn and Wassermann tests were positive and a positive TPI (*Treponema pallidum* immobilization) test was also obtained. The luetic infection was treated with eight million units of penicillin, but her chronic urinary tract infection recurred despite numerous courses of antibiotic therapy. Difficulty in controlling the blood pressure was experienced as attempts to lower the supine blood pressure by reducing the amount of 9-α-fluorohydrocortisone resulted in severe postural hypotension. The patient was admitted to hospital on June 19, 1956, at 31 weeks' gestation because of these problems in management and for investigation of adrenal cortical steroid metabolism. Treatment in hospital failed to produce improvement and a persisting albuminuria with a slightly elevated NPN developed. At 34-35 weeks' gestation, it was decided to terminate the pregnancy because of progressive albuminuria and a rising NPN. On July 12, 1956, the patient felt a diminution of fetal movement and on the next day did not experience any fetal movement at all. At that time the fetal heart sounds could not be heard and the infant was lying transversely with the presentation resistant to conversion to a longitudinal lie. The cervix was long and closed and it was felt that because of the abnormal presentation and fetal distress, Cesarean section was indicated. This operation was performed under local anesthetic and a stillborn male child weighing 4 lb. 12 oz. was delivered. The patient's immediate postoperative condition was satisfactory, but on her fourth postoperative day she showed signs of shock and blood loss due to extensive hemorrhage into the intestinal tract. This was managed by replacement transfusion and the bleeding subsequently subsided. Radiological investigation of the upper and lower gastrointestinal tract showed no evidence of any lesion. The patient was discharged from hospital on August 29, 1956.

She was readmitted in November 1956 for acute bronchitis and chronic pyelonephritis. In August 1957 she was again readmitted because of peripheral vascular disease and arteriosclerotic gangrene of the left great toe. A lumbar sympathectomy and exploration of the left popliteal artery with periarterial sympathectomy failed to arrest the process and ultimately the patient required a transmetatarsal amputation of the left foot. The patient was readmitted with bronchopneumonia in May 1959 and again in September 1959. She died as a result of acute pulmonary edema and cardiac failure on October 2, 1959. Postmortem ex-

amination showed a recent myocardial infarct, chronic pyelonephritis and nephrosclerosis.

CASE 2 (Mrs. N.B.).—This 32-year-old woman was admitted to the Toronto General Hospital on October 17, 1955. She gave a history of fatigue, easy bruising of the skin, acne, hirsutism, back pain, swelling of the hands and feet, and amenorrhea of 10 months' duration Her obstetric history revealed that she had had four male infants, the last having been born in January 1955. She had continued to nurse this infant until May 1955. Prior to admission to hospital she had had no menstrual period since her last pregnancy. A clinical diagnosis of Cushing's syndrome was confirmed by the demonstration of high levels of urinary 17-ketosteroids and 17-hydroxycorticoids, and a hyperactive response to intravenous ACTH. On November 9, 1955, a bilateral total adrenalectomy was performed. The pathological diagnosis was bilateral hyperplasia, the total weight of both adrenals being 20 g. Her postoperative course was satisfactory and the stigmata of Cushing's syndrome gradually disappeared. Therapeutic stabilization was reached with 25 mg. cortisone and 0.2 mg. of 9-α-fluorohydrocortisone daily. Her menstrual periods returned in January 1956, and she experienced two normal periods in February and on March 22, 1956. Following this she became pregnant; the expected date of confinement was December 29, 1956. On January 5, 1957, the patient was delivered by outlet forceps of a 6 lb. 11 oz. female child. No complications were encountered ante or post partum. Her labour was of six hours' duration. During labour the patient was managed by intramuscular injections of 100 mg. of hydrocortisone hemisuccinate.

The patient was followed through a second pregnancy in 1959. Her last menstrual period was on May 23, 1958, with the expected date of confinement on March 2, 1959. On March 3, 1959, a female child weighing 7 lb. 9 oz. was spontaneously delivered. Labour was induced by low rupture of the membranes and began two hours after this procedure. The total duration of labour was five hours and 28 minutes. During labour the patient received three doses of hydrocortisone hemisuccinate intramuscularly, totalling 200 mg. In the postpartum period a mild pyelonephritis developed, but this responded promptly to antibiotic therapy. No other complications were encountered. The patient was discharged in good health on hydrocortisone 20 mg. and 9-α-fluorohydrocortisone 0.1 mg. daily.

CASE 3 (Mrs. B.B.).—This 21-year-old married woman was admitted to the Toronto General Hospital on August 30, 1956. She gave a history of attacks of fainting for the previous four weeks and loss of 40 lb. in weight in the previous eight months. In addition she had been aware of increasing fatigue and frequent headaches. Her menstrual periods had remained normal in amount but had decreased slightly in frequency from every four weeks to approximately a five-week cycle. Examination showed areas of brownish pigmentation on the face and in the mucus membrane of the mouth. Her blood pressure was 84/50 mm. Hg, in the recumbent position, and 60/40 standing. From ACTH stimulation tests there was no evidence of adrenal cortical response. A diagnosis of Addison's disease was made and the patient was discharged on cortisone 12.5 mg. three times daily. In September 1957, the patient was readmitted to hospital with an addisonian crisis due to a respiratory infection and failure to take cortisone regularly. This responded satisfactorily to treatment and she was discharged four days later on a maintenance dose of 25 mg. of cortisone daily. The patient became pregnant shortly afterward, her last menstrual period being September 20, 1957, with an expected date of confinement on June 27, 1958. Her prenatal course was uncomplicated and she was delivered, by low forceps, of her first child on June 21, 1958, after a labour of six hours and 24 minutes. The infant was a male child weighing 6 lb. 14 oz. Hydrocortisone hemisuccinate, 100 mg., was given intravenously and 100 mg. intramuscularly during labour. Cortisone therapy was reduced progressively and the patient was discharged from hospital on June 28, 1958, on doses of cortisone 25 mg. and 9-α-fluorohydrocortisone 0.1 mg. daily.

CASE 4 (Mrs. E.M.).—A 30-year-old Indian woman was admitted to the Toronto General Hospital on October 31, 1958, for investigation. She gave a six-year history of obesity with a weight gain of 45 lb., from 140 to 185 lb. In the past two years she had noted an increase of facial and chest hair with marked acne. During the same period she had moderately severe lumbosacral backache and headache. One year previously a diagnosis of Cushing's syndrome had been made but there had been no further follow-up treatment. She had two previous pregnancies: one, six years earlier with a surviving child, and one neonatal death 12 years ago. The menses had been slightly irregular over the past five years. On examination she showed a rounded, "moon face", with obesity of the trunk. There was marked increase of facial hair, with acne. Her blood pressure was 140/90 mm. Hg and no striae were evident. There was mild glucosuria and the blood sugar level was slightly elevated. An intravenous pyelogram and skull radiographs were normal. Her 17-hydroxycorticoids ranged between 13 and 22.4 mg. per 24 hours, and her urinary 17-ketosteroid excretion ranged between 15.4 and 27.4 mg. per 24 hours. ACTH intravenous stimulation resulted in a slightly increased response.

On December 1, 1958, a total bilateral adrenalectomy was performed. Her postoperative state was uncomplicated and the pathological diagnosis was hyperplasia of the adrenal glands; the combined weight of the glands was 18 g. The patient was discharged from hospital on December 20, 1958, on cortisone acetate 25 mg. twice a day and 9-α-fluorohydrocortisone 0.1 mg. daily. The patient had no menses following her operation, experienced a loss of 20 lb. in weight and felt considerably improved. There was diminution of the facial hair and acne. Her blood pressure was 130/80 mm. Hg. The patient responded to an estrogen withdrawal test on March 30, 1959, and subsequently had no further periods. Pregnancy was diagnosed, with the estimated expected date of confinement about mid-February 1960. On January 16, 1960, the patient went into spontaneous labour and in four hours and 55 minutes spontaneously delivered a female child weighing 5 lb. 10¾ oz. Delivery was carried out under general anesthesia and the baby was weaned. During her labour the patient received 200 mg. of intramuscular hydrocortisone hemisuccinate in divided doses. In the

postpartum period the patient complained of some manifestations of postural hypotension, but on readjustment of the dosage of steroids this was satisfactorily controlled. She was discharged from hospital on January 31, 1960, on 40 mg. hydrocortisone and 0.1 mg. 9-α-fluorohydrocortisone daily.

CASE 5 (Mrs. J.D.).—This 34-year-old married woman was admitted to the Toronto East General Hospital on January 27, 1959. From her history it was rather difficult to be sure of the exact onset of her illness. She had developed roundness and fullness of the face over the past seven years and had exhibited a tendency to bruise easily for a considerable period of time. In the five years prior to admission to hospital she had gained 20 lb. in weight, from 115 to 135 lb. However, this had been reduced on dietary management to 117 lb. She had, however, been unable to get rid of the fat pad at the back of the neck. She felt that she was hyperactive, nervous and somewhat irritable. In June 1958 she had developed swelling of the ankles. This had progressively increased and she had developed fatigue, acne, occasional headaches, dorsal back pain, shortness of breath on exertion, and loss of libido. There had been a decrease in breast size and her periods had become irregular and rather scant. Mild hirsutism was present. On examination she was an anxious, apprehensive woman with a red "moon face", mild hirsutism and a buffalo-hump. Her eyes were prominent. Her blood pressure was 160/110 mm. Hg. There were no abdominal masses or striae. She had a mild anemia of iron deficiency type. Her urinary 17-hydroxycorticoids ranged between 13.4 mg. and 18.2 mg. per 24 hours. The 17-ketosteroids were also elevated, ranging between 36 and 38 mg. per 24 hours. On ACTH stimulation her 17-hydroxycorticoid excretion showed an increased response, as did the 17-ketosteroid excretion. Skull radiographs and an intravenous pyelogram were normal.

A diagnosis of Cushing's syndrome was made and on February 10, 1959, a bilateral total adrenalectomy was performed. Her postoperative course was uneventful. The combined adrenals weighed 18.5 g., and the pathological report described adrenal hypertrophy and hyperplasia. The patient was discharged on 25 mg. of cortisone twice a day. In addition she was given 9-α-fluorohydrocortisone 0.1 mg. daily.

The patient became pregnant for the first time in July 1959, with an expected date of confinement of April 19, 1960. In her antepartum course she showed a weight gain of 17 lb. (115-132 lb.) and exhibited an intermittent slight hypertension of 140-150/90 mm. Hg. While in hospital for investigation she spontaneously went into labour on April 13, 1960, at 39 weeks' gestation. The duration of her labour was two hours and four minutes, and the baby was delivered by low forceps with the use of a general anesthetic. The placenta was retained and was manually removed. The infant, a female child, weighed 4 lb. 14½ oz. Its condition was good and it continued to improve to the time of discharge from hospital. During labour the patient received two 100-mg. doses of hydrocortisone hemisuccinate. By diminishing the dose of the steroid, maintenance therapy was established on cortisone 25 mg. twice a day and 9-α-fluorohydrocortisone 0.1 mg. daily. Investigation in the postpartum period of this patient's steroid excretion suggested that there was a small remnant of adrenal cortical tissue left. There was, however, failure of any response to stimulation by an intravenous ACTH test. The patient was discharged without steroid therapy, with instructions that if an episode of stress occurred it would be necessary to resume such treatment. The patient did not feel well without steroid therapy, so this was reinstituted shortly after her discharge from hospital.

COMMENT

Four patients with bilateral total adrenalectomy for Cushing's syndrome were followed through five pregnancies. All patients received adequate adrenal cortical steroid therapy to meet their needs. Only one patient presented major complications, a 40-year-old woman with longstanding hypertension and chronic pyelonephritis. The complications were essentially due to these factors complicated by a transverse lie with fetal distress at 34-35 weeks' gestation. After Cesarean section this patient showed a rising NPN level and depressed renal function and on her fourth postoperative day manifested bleeding from the bowel that persisted over the next week. However, with conservative treatment the bleeding stopped and the patient improved. One other patient developed mild pyelonephritis in the postpartum period and this responded readily to antibiotics. Two patients showed evidence of postural hypotension and required readjustment of their dosage of 9-α-fluorohydrocortisone. Two of the patients had slight edema of the ankles and hypertension. One woman with Addison's disease was managed throughout pregnancy and delivered without complication. One patient (Case 5) was considered on postpartum investigation to have a remnant of adrenal cortical tissue left, although total bilateral adrenalectomy had been previously performed. However, it was not found possible to maintain this patient in a satisfactory state without substitution therapy.

During labour all patients were treated with parenteral hydrocortisone as indicated and this was gradually diminished in dosage and converted to oral therapy in the postpartum period.

The only major complications encountered in this group of patients occurred in Case 1; these resulted from longstanding hypertension and chronic renal disease. This observation is in keeping with the view expressed by Hunt, that complications in patients with treated or untreated Cushing's syndrome are chiefly related to existing hypertension.

All patients with Cushing's syndrome in this series were treated surgically by bilateral total adrenalectomy. The advent of potent steroid substitution therapy with its diminishing expense has rendered total adrenalectomy preferable to subtotal adrenalectomy. The problem of management of patients with subtotal adrenalectomy was encountered in one case reported by Schneider, Weed and Bowers,[16] and in the case described by Tivenius.[18] Both of these patients with subtotal

adrenalectomy required subsequent total adrenalectomies for recurrence of Cushing's syndrome.

Studies on the activity of aldosterone and hydrocortisone in these patients have been reported elsewhere by Laidlaw, Cohen and Gormall,[10, 11] who found minor amounts of aldosterone during the third trimester of pregnancy in two of these patients. This suggested that the placenta or the fetal adrenal cortex or both may be a source of small amounts of aldosterone during pregnancy. It was concluded, however, that not more than one-tenth of the average excretion of aldosterone by normal pregnant women in the third trimester of pregnancy could be detected in these adrenalectomized patients. Consequently, the major source of urinary aldosterone during pregnancy must be sought outside the placenta or the fetal adrenal. In respect to hydrocortisone, it was concluded that the rise in the level of plasma hydrocortisone during pregnancy was chiefly due to a diminished rate of transformation of hydrocortisone to certain of its metabolites and to a greater retention of the hormone within the intravascular compartment.

SUMMARY

Six pregnancies were followed in five patients with absent adrenal cortical function. Four of the patients had undergone bilateral adrenalectomy for Cushing's disease; the fifth had Addison's disease.

Although the number of patients is small, it is felt that because of the infrequency with which such cases are described in the medical literature, this group of patients is worth reporting.

Investigation of the metabolism of hydrocortisone and aldosterone in these patients has been reported elsewhere.

From the obstetrical standpoint, no major complications were encountered following the loss of adrenal cortical function. Periodic readjustment of the doses of adrenocortical steroids was necessary. The commonest problem encountered was postural hypotension. While this could be overcome by increasing the amount of administered adrenocortical steroids, there was a tendency for hypertension to develop with too high a dose.

Labour was conducted normally in five of the six cases. One patient was delivered by Cesarean section at 34 weeks' gestation because of progressive hypertension, chronic pyelonephritis and fetal distress. This infant did not survive, but the other five were normal.

During labour, adrenocortical steroids were given parenterally. No significant abnormality of labour or the puerperium was encountered in the absence of adrenocortical function when replacement therapy was properly regulated.

All five of the patients reported on were investigated and managed through pregnancy by Dr. John C. Laidlaw of the Department of Medicine of the University of Toronto and the Toronto General Hospital. It was through his kind co-operation that these patients were referred to the Department of Obstetrics for prenatal care and delivery. Thanks are also extended to Drs. W. T. W. Clarke and E. G. Cross for referring their cases to Dr. Laidlaw for investigation and inclusion in this study.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

We must remember that we have at least two distinct methods of tuberculous invasion: first, a bronchogenic type, which occurs in a small majority of cases, and is usually quickly fatal. I wish most emphatically to distinguish this type from pulmonary tuberculosis of lymphatic infection, which constitutes probably ninety-five per cent. or more of the pulmonary tuberculosis in this country. Incipient pulmonary tuberculosis is the beginning of lung disease, but it is not the beginning of tuberculosis. Where, then, do we get this infection? One who has tuberculosis, evidenced by an apical infiltration, and breaks down, can, upon looking backward, see as it were down a long lane, highly walled with trouble on each side,—spring and fall colds and unaccountable fevers,—until finally the resistance is broken by a bad environment and the enemy begins to win the game. "Every man eats a peck of dirt," and I have no hesitation in saying that the larger part of the peck is eaten in early childhood when the babies are on the floor. Whether they get it from polluted milk, food, or general household dirt, it matters not, infection takes place and, according to the resistance of the child, either kills him quickly or becomes latent in some part of the lymphatic system. Theoretically we can trace these organisms passing in the alimentary canal into the mesenteric lymphatic system, each gland involved in succession, fighting against the invasion which slowly works upwards through the mediastinal lymphatics, and ultimately comes to rest at the apex of one or both lungs, where, the lymphatic stream being exceedingly slow, and the lung excursion very limited, fine adhesions are formed and a nesting place found. By this time the child has graduated from indoors and leads a happy, outdoor life, with good food and fresh air, but nevertheless the enemy still lurks in the system, and in early adult life when the candle is being burned at both ends, environment breaks the resistance, the disease becomes active, and infiltration in the pulmonary tissue begins.—Discussion, Section of Medicine, 44th Annual Meeting of the Canadian Medical Association, *Canad. M. A. J.*, 1: 625, July 1911.

AN EPIDEMIC OF ASEPTIC MENINGITIS CAUSED BY COXSACKIE B TYPE 2 VIRUS*

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THROUGH the years Coxsackie B viruses have been present in different communities, but there has been a constant variation in the type causing each epidemic.

Curnen[1] reported that in North Carolina, in successive years, there have been noteworthy variations in type. Coxsackie B1, prevalent in New York and New England during 1947 and 1948,[2-5] has occurred only sporadically in the rest of the United States and has not been isolated by him since 1949. On the other hand, Coxsackie B4 has been found every year, with a definite increase in 1957. Coxsackie B5, as reported elsewhere in the United States and Canada,[1, 3, 6, 7] was far the most common in 1957. The following year Curnen found the same number of B3, B4 and B5, and it was only in 1959 that he came across a series of B2 even though the incidence of B5 did not change for that year.

Cooper *et al.*[8] reported that in the Province of Ontario, during the 1957-1959 period, there were many isolations of Coxsackie B5. Coxsackie B2 appeared in considerable numbers for the first time in 1959, isolated mostly from cases of aseptic meningitis.

During the summer of 1959 in the Institute of Microbiology and Hygiene of the University of Montreal, 247 Coxsackie B5 strains and no Coxsackie B2 strains were isolated. It is interesting to note that at that time Coxsackie B2 was as frequent as Coxsackie B5 in the Province of Ontario.[6, 8] During the summer of 1960 Coxsackie B5 was not isolated in the virus laboratory of the Institute though Coxsackie B2 was frequently isolated.

In June 1960 a number of patients with aseptic meningitis presented with unusually severe abdominal or chest pain in association with sore throat. The present report describes the clinical and laboratory findings of this epidemic.

MATERIALS AND METHODS

After Coxsackie B2 had been isolated during routine virus studies on a few patients with aseptic meningitis in June 1960, a systematic study of all cases of aseptic meningitis admitted to the Montreal Children's Hospital was undertaken.

Application of rectal swabs and throat swabs and removal of spinal fluid and serum were carried out on admission. A second sample of blood was taken during convalescence. Swabs were rapidly agitated in small screw-capped tubes containing 1-2 ml. of M150 media, with 625 micrograms (μg.) of penicillin and 200 μg. of streptomycin per ml., and were then stored at –20° C.

After thawing, 0.1 ml. of each specimen was inoculated into each of three culture tubes of rhesus kidney and HeLa cells. The cells were examined daily for 14 days for the appearance of cytopathic effects. When these appeared, the supernatant fluid was harvested and again passaged before further identification could be made. Maintenance media consisted of M150 for monkey kidney cells, while 5% calf serum was added to the HeLa cell line.

The neutralization tests were performed in the usual manner by using the patient's sera diluted with M150 media and inactivated for 30 minutes at 60° C. Four dilutions of both the acute and the convalescent sera were made from 1/16 to 1/1024 and mixed with an equal volume of known virus diluted to contain 100 $TCID_{50}$ per 0.1 ml. The mixtures were kept at room temperature for a period of at least 75 minutes. Then each of four culture tubes of monkey kidney cells was inoculated with 0.2 ml. for each dilution of serum. The tubes were incubated at 37° C. in roller drums and examined daily until typical cytopathic effects appeared in the tubes harbouring the control virus. The titre of neutralizing antibodies was calculated by Kärber's method.

CLINICAL OBSERVATIONS

From late June until early October 1960, 61 patients were seen. Only seven were encountered in July, 17 in August, 23 in September and five in October. The incidence of meningitis caused by Coxsackie B2 virus seemed to follow that of poliovirus during the same period (Fig. 1). A seasonal distribution is strikingly similar for all enteroviruses.

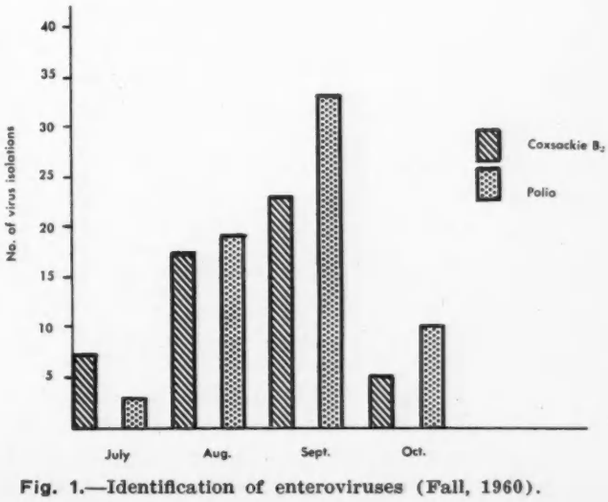

Fig. 1.—Identification of enteroviruses (Fall, 1960).

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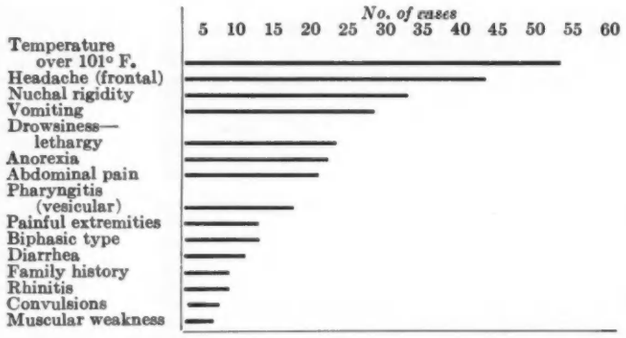

Fig. 2.—Symptomatology in 61 cases in which Coxsackie B2 virus was isolated (Fall, 1960).

The clinical findings are presented in Fig. 2. Fever was present in 54 cases. The six cases without elevated temperature occurred in four contacts in a family where four younger children and three older ones were sick; some siblings excreted the virus but were not affected subjectively by it; the others did not record their temperature. Of the 43 patients reporting some form of headache, 20 described it as being of the constricting type. It was present before the onset of meningeal signs and lasted throughout the febrile period. More than half showed evidence of nuchal rigidity on examination.

TABLE I.—AGE DISTRIBUTION OF PATIENTS WITH COXSACKIE B2 INFECTION

Age	*No. of patients observed*
Up to 1	6
1 - 5	13
6 - 10	15
11 - 14	12
15 and over	12

Abnormal spinal fluid was found in all cases, and of the 34 for whom a cell count was recorded only two showed cell counts exceeding 1000 per ml. The cells were predominantly lymphocytes, except in cases where the spinal tap was performed early in the illness, when there was a predominance of polymorphonuclear leukocytes. The highest protein content of the spinal fluid was 77 mg. %.

Vomiting, accompanied by headache, was observed but it was not projectile and appeared mostly in the febrile phase of the disease. Drowsiness and lethargy were quite pronounced early in the disease and complete recovery often took many days. In five instances there was some guarding, with localized tenderness in the right lower quadrant. The abdominal pain was severe enough, in a few instances, to justify surgical consultation. Fortunately, operation was not considered necessary in any case, and by the next day the pain had disappeared. Usually present with the abdominal pain was a history of sharp chest pain, usually unilateral and increasing with deep inspiration. This was found predominantly in the older group of patients. Quite severe diarrhea occurred in 10 cases, always in children under six years of age. No evidence of blood in the stools was reported. In 14 instances an episode of similar symptoms was reported two to four weeks previously but without involvement of the central nervous system.

In none of these patients were the physical findings impressive. Even with 1000 cells in his spinal fluid and a temperature of 104° F., one child showed no obvious distress except for mild discomfort caused by a severe headache. No rashes were encountered in this series. The only positive findings were those of meningitis and a rather distinctive pharyngitis. The pharynx was usually very red, sometimes granular, showing a crop of small vesicles on the anterior pillars of the soft fauces, on each side of the uvula, not unlike those seen in herpangina. The rest of the buccal mucosa was not involved. There were no cases of frank paralysis, but six patients presented with transient muscle weakness which disappeared within a few weeks. Generalized convulsions, none lasting for more than 10 minutes, were reported in seven cases.

Although the studies included adults and children, the infection occurred predominantly among the latter (Table I).

TABLE II.—VARIETY OF MANIFESTATIONS IN ONE HOUSEHOLD AFFECTED WITH COXSACKIE B2 VIRUS

			Clinical findings		*Virological findings*	
Name	*Age*	*Onset*	*Subjective*	*Objective*	*Isolation Coxsackie B2*	*Neutralizing antibodies*
R.A.	17 years	July 4, 1960	Cough, malaise, neck and chest pain, headache	Temp. 100° F., pharyngitis, stiff neck and back	+	10 50
M.A.	18 years	July 4, 1960	Pain in (R) chest, headache, anorexia	Pharyngitis, rales in chest, temp. 100° F.	+	— —
J.L.A.	11 years	July 8, 1960	Headache, drowsiness, chills	Pharyngitis, temp. 103° F., CNS +	+	>512 256
R.A.	3 years	July 9, 1960	Headache, back pain, vomiting	Pharyngitis, temp. 103° F., CNS +	+	45 64
C.E.A.	5 years	July 21, 1960	Headache, abdominal pain	Temp. 100° F.	+	— —
C.A.	20 years	July 21, 1960	Headache, chest and back pain, sore legs	Temp. 101.4° F., nystagmus, CNS +	0	10 30
P.A.	6 years	August 1, 1960	None	Temp. 99.2° F.	+	44 512
D.A.	4 years	August 1, 1960	None	Enlarged red tonsils	0	128 >1024
J.S.	8 months	August 1, 1960	None	Enlarged red tonsils	+	— —

TABLE III.—VIROLOGIC FINDINGS IN 61 CASES OF INFECTION WITH COXSACKIE B2 VIRUS

Case No.	Neutralizing antibodies for Coxsackie B2		Isolation of Coxsackie B2 virus		
	1st	2nd	Rectal swab	Throat swab	CSF
1	—	8096	+		
2	512	255	+		
3	45	64	+		
4	—	—	+		
5	44	512	+		
6	128	1024	0		
7	—	—	+		
8	512	354	+		
9	125	707	+		
10	—	—	+		
11	45	22	+		
12	—	—	+		
13	—	—	+		
14	—	—	+		
15	177	128	+		
16	45	2048	+		
17	16	16	+		
18	32	1024	0		
19	—	—	+		
20	64	89	+		
21	—	—	+		
22	0	64	+*		
23	45	354	0		
24	32	64	+		
25	45	250	+		
26	0	256	0	•	
27	—	—	+		
28	—	—	+		
29	22	256	+		
30	—	—	+		
31	0	89	+	+	
32	45	512	+	+	
33	16	32	+		
34	32	64	+	+	
35	—	—	+		
36	178	707	+		
37	64	355	+		
38	—	—	+		
39	—	—	+		
40	—	—	+		
41	89	707	+		
42	128	740	+		
43	—	—	+		
44	45	512	+		
45	11	355	+		
46	22	125	+		
47	32	355	+		+
48	256	1024	+		
49	256	740	0		
50	16	89	+		
51	128	89	+		
52	—	—	+		
53	0	32	+		
54	—	—	+		
55	—	—	+		
56	—	—	+		
57	—	—	+		
58	—	—	+		
59	16	11	+		
60	256	256	+		
61	—	—	+		

*Suckling mice showed lesions compatible with Coxsackie B virus infection.

In different members of one family or of a community, Coxsackie B2 virus can induce a varied spectrum of symptoms. This was the case in the first family where Coxsackie B2 was isolated (Table II).

Of 12 persons living in the same household, only the mother and both maternal grandparents did not show evidence of Coxsackie B2 infection. All the children, ranging in age from eight months to 20 years, were affected. Six were hospitalized with aseptic meningitis, but one of them did not present with a positive spinal fluid, although he had the same severe abdominal pain and vesicular pharyngitis. None of the remaining three had any complaints, but on examination two were found to have enlarged red tonsils and a temperature of 99.2° F. They all had evidence of Coxsackie B2 infection either by isolation of the virus or by an increase in neutralizing antibodies.

VIROLOGICAL STUDIES

Coxsackie B2 virus was isolated in 55 cases (Table III). Most frequent isolation of the virus was obtained from rectal swabs (Table IV), while 15 throat swabs were positive in only three cases. In one infant Coxsackie B2 virus was isolated from the cerebrospinal fluid as well as from the rectal swab (Case 47). The lumbar puncture in this case was performed 12 hours after the appearance of the meningeal signs. General malaise and muscular pain had already been present for one week. At the time of admission the spinal fluid contained 34 cells; 24 hours later this number had increased to 524 cells of which 471 were lymphocytes.

TABLE IV.—IDENTIFICATION OF COXSACKIE B2 VIRUS

Total number identified	Feces	CSF	Throat	Mice	Serology only	Serology: tissue culture
61	50	1	3	1	6	32

In one case no virus was isolated on tissue culture from the rectal swab, but the same specimen inoculated into suckling mice produced lesions compatible with those caused by Coxsackie B virus. In the patient's sera an increase of neutralizing antibodies against Coxsackie B2 virus from 0 to 1/64 was measured.

A fourfold increase in neutralizing antibodies was observed in 32 cases in which Coxsackie B2 had been isolated. The remaining 12 all had presented antibody levels which increased twofold or less. Six cases in which virus was not isolated have been included in the series, since a significant increase in the neutralizing antibodies along with a typical history could be shown. In all, 61 cases were identified (Table IV) as Coxsackie B2 infection.

In all cases where serum was available it was tested for neutralizing antibodies against the three types of poliovirus. In no instance could an increase in poliovirus antibody be demonstrated. One patient had a Coxsackie B2 virus isolated from a rectal swab specimen and also showed a positive titre of 1/181 and 1/91 against Poliovirus type 1. He had no neutralizing antibodies against Poliovirus types 2 and 3 or against Coxsackie B2 virus. This particular patient had not been vaccinated, was nine months of age and had been admitted to hospital with a flaccid paralysis of one extremity; one can safely assume that the responsible agent was Poliovirus type 1 and that the Coxsackie B2 virus isolated in the feces (and not present in the throat or the cerebrospinal fluid) was an intestinal cohabitant.

DISCUSSION

It is well established that Coxsackie B virus is one agent responsible for aseptic menigitis.[7, 9] This virus has been isolated from the spinal fluid of many such patients.[9, 10] Shelokov[11] reported one case where a Coxsackie B2 virus was recovered from the blood of a physician who developed aseptic

meningitis a few days later. In all these cases a careful search for the poliovirus was made without success. Horstmann[12] has shown that the Coxsackie virus was not a normal inhabitant of the intestinal flora. She also showed their potentiality in producing central nervous system lesions in the rhesus monkey.[13]

From late June until early October 1960, 61 cases of illness caused by Coxsackie B2 were studied. From these, more than half presented the picture of aseptic meningitis. In 32 cases with a typical history, a virus was isolated during the acute phase and a fourfold increase in neutralizing antibodies between the acute and convalescent phase was demonstrated (Tables III and IV). In one instance it was possible to demonstrate the presence of Coxsackie B2 in the spinal fluid. Not one Coxsackie B2 virus was isolated in all the diagnostic work carried out in the virus laboratory of the Institute, for respiratory or unrelated illnesses.

To rule out poliovirus as the cause of aseptic meningitis, paired sera were studied for neutralizing antibodies in 38 cases. All the results were negative.

Judging from the numerous reports received from practising pediatricians, this clinical picture was prevalent all around Montreal and this represents only a few cases showing evidence of aseptic meningitis that were studied thoroughly. Many cases were also identified in other hospitals where viral isolation showed Coxsackie B2 as the etiological agent.[13]

It is not common to find Coxsackie B2 virus as the causative agent of an epidemic but in 1958 it was found to be the responsible agent in a group of dependants of military personnel at a large naval training station in the Great Lakes region.[15] Of 361 individuals tested, 35 Coxsackie B2 virus was isolated from 78% of a total of 45 patients from whom enteroviruses were recovered. The other 10 viruses were equally divided between Adenovirus type 1, ECHO virus, poliovirus and Coxsackie B3. This group had the same clinical findings as those encountered in the present series, except for the meningeal involvement.

Every summer the clinician is faced with the same question whether a case of aseptic meningitis is poliomyelitis or not. With the present widespread use of poliomyelitis vaccine it is more important than ever to establish wherever possible an exact etiological diagnosis in every child who presents with aseptic meningitis with or without paralysis, employing all the facilities of the modern virus laboratory.

CONCLUSIONS

Clinical and virological findings during an epidemic of aseptic meningitis due to Coxsackie B2 virus in and about Montreal have been reported.

Unusual features in this epidemic were the type of pharyngitis and the abdominal and chest pain preceding or accompanying the meningeal signs.

The viral etiology was proved in over 50% of the cases by virus isolation and demonstration of neutralizing antibodies.

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RÉSUMÉ

Depuis la fin de juin 1960 jusqu'au début d'octobre de la même année, 61 cas de maladie fébrile due au virus de Coxsackie B2 ont été étudiés. Plus de la moitié ont présenté une image de méningite aseptique sans paralysie permanente alors que les autres n'avaient que des malaises généraux avec céphalée intense, douleur thoracique unilatérale aggravée par l'inspiration profonde, ou une douleur abdominale aiguë, périombilicale, le tout ne durant pas plus de 5 jours mais pouvant présenter une rechute au bout de deux semaines.

Chez 54 d'entre eux le virus a pu être isolé du lavage de gorge ou des fèces et chez un enfant on a pu l'isoler du liquide céphalo-rachidien. Chez 32 enfants on a pu démontrer une augmentation significative des anticorps neutralisants.

A l'examen physique de ces malades on notait une pharyngite vésiculeuse comme celle de l'herpangine mais sans passer au stade d'ulcérations. Les poumons et l'abdomen n'offraient rien d'objectif.

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

The corner-stone of the new building of the Montreal General Hospital was laid by His Excellency the Governor-General on June 6. This building is the first of a series which are projected to replace those now in use. The date was well chosen, as on June 6, 1821, ninety years ago, the corner-stone of the present hospital was laid, with considerable pomp and ceremony, by Sir John Johnson.

During the week beginning June 5, and preliminary to the meeting of the Canadian Medical Association, a reunion of the graduates of McGill University in the medical faculty was held at Montreal. About six hundred graduates were present. They were entertained by ten members of the teaching staff at a banquet, and various class dinners were held. The presence of so many physicians assembled for a special purpose accounts in some degree for the large attendance at the meetings of the Association.—*Canad. M. A. J.*, 1: 680, 1911.

CLINICAL STUDY OF A POTENT ANTIDEPRESSANT, TRANYLCYPROMINE WITH TRIFLUOPERAZINE (PARSTELIN*), IN THE AGED CHRONICALLY ILL

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DEPRESSIVE illness is by far the commonest and most challenging problem that confronts the modern psychiatrist,[1, 2] yet the manifestations of depressive reactions are so protean that missed diagnosis is still very common. The latter situation is especially more likely to occur when one is dealing with an aged population, particularly when chronic illness is also present. The tendency then exists to concentrate on the organic disease alone, or to fail to recognize that the somatic disorders may exist as depressive equivalents.

Hayes[3] recently called attention to the fact that even among admissions to a mental hospital, many patients have underlying depressive pathology which is not readily apparent or easily uncovered, so that appropriate treatment measures may not be instituted.

One of the authors of this report[4] has called attention to the frequency of depressive reactions in the aged chronically ill group. Such depressions are related to the state of the chronic illness when there is accompanying limitation of function or pain.

Depression also accompanies the psychological regression which arises from the inability to work and to be economically self-sufficient, or it may develop from the environmental and emotional dislocation of the aged person. The latter conditions develop as a consequence of the increasing exclusion of the aged ill person from ego-sustaining relationships within the family and community.

A meaningful expression of the basic unity of geriatric psychiatry and geriatric medicine is provided by a recently completed study at the Jewish Hospital of Hope, Montreal. In a one-year study of 115 patients who were admitted to this hospital for the care of chronic diseases and who were screened prior to admission to exclude the mentally ill, 90% of the patients were discovered to be suffering from a diagnosable psychiatric illness.[5] The awareness of the need for active treatment of the depressed reactions in this group has been previously reported in a study on the use of imipramine (Tofranil).[6] The latter drug was found to be ineffective in this patient group, and the lack of therapeutic response was considered to be a reflection of the organic contaminants of the depressed reaction. However, the search for a useful pharmacological antidepressant has been continued, and a more successful clinical trial can now be reported with the use of tranylcypromine with trifluoperazine (Parstelin). The report on this drug study forms the basis of the present paper.

Tranylcypromine with trifluoperazine has only very recently been reported as an effective rapid-acting antidepressant with few side effects.[7-9] These preliminary reports describe trials in a mental hospital group and refer also to the high degree of effectiveness in an ambulatory patient group from private practice. As far as we are aware, the present report is the first to describe the drug effects in a group where the depressed reactions and other psychological disorders are complicated by organic disease and also by old age.

PHARMACOLOGY

One tablet of Parstelin contains 1 mg. of trifluoperazine (Stelazine) and 10 mg. of tranylcypromine (Parnate). Administered to dogs anesthetized with pentobarbital, this combination lowered blood pressure, reversed the pressor effects of adrenaline, and inhibited the ganglionic effect of dimethyl phenyl piterazinium iodide (D.M.P.P.), thus indicating ganglionic blocking activity. Parstelin is a monoamine oxidase inhibitor, affecting both serotonin and noradrenaline metabolism. Trifluoperazine is clinically established as a potent phenothiazine, and tranylcypromine is a potent psychic energizer.

PROCEDURE

The Jewish Hospital of Hope in Montreal is an accredited institution for the treatment of the chronically ill. Many patients are aged at the time of their admission. The existing criteria exclude from admission those who have a presenting mental disorder, but our findings nevertheless indicate that approximately 90% have a diagnosable psychiatric disturbance in spite of the attempt to screen out the mentally ill patient before admission.

Our drug study involved a total of 44 hospitalized patients. Excluded from the test group were those with severe irreversible dementia and those with disorders requiring continuous therapy with other drugs.

The period of observation lasted three months. The initial dose of tranylcypromine with trifluoperazine (Parstelin) was one tablet twice daily, administered orally, on waking and after lunch. Adjustments of the dosage upwards or downwards were made on the basis of clinical assessment. Before the experiment was begun all other medication was discontinued and none was given except for essential need during the drug trial. Each patient had a complete hemogram, non-protein nitrogen and alkaline phosphatase estimation prior to the drug administration and also at the termination of the trial, whenever that happened to be for the individual patient. Each patient also had a full psychiatric evaluation before and after such

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TABLE I.—PARKINSON'S DISEASE

Number	Name	Age years	Sex	Duration of hospitalization	Associated physical disease	Reaction			Complications and side effects
						Excellent	Good	Poor	
1	D.P.	58	F	216 mos.	Post-encephalitis			X	Increased seizures
2	W.W.	68	M	54 mos.	Prostatism			X	Increased confusion
3	M.A.	78	M	17 mos.	Chronic brain syndrome			X	Increased stiffness
4	A.D.	63	M	12 mos.	Chronic brain syndrome			X	Increased tremors
5	B.K.	67	F	42 mos.	Chronic brain syndrome			X	Drug rash
6	L.D.	53	F	82 mos.	Post-encephalitis		X		Nil
7	J.A.	78	M	12 mos.	Arthritis, chronic brain syndrome	X			Nil
8	B.M.	59	M	5 mos.	Diabetes, post-encephalitis			X	Increased confusion

treatment, but the specific psychiatric data and diagnosis were not disclosed until the drug study was completed and after all the available clinical and observational test data had been recorded. Clinical observations were made by multiple observers. These included the medical superintendent, two members of the resident staff, two psychiatrists and the superintendent of nurses. Thus five medical personnel and ancillary staff members contributed data on each patient. A chart was kept for comments on individual items such as changes of food intake, sleep, complaints, activity and cooperation. These objective data were added to the subjective impressions of the patients and to the clinical assessments made by the trained observers. Weekly urinalyses were also carried out on each patient and a blood pressure record was maintained from the start to the end of the drug trial. Side effects observed by others or complained about were also charted.

TABLE II.—CHRONIC BRAIN SYNDROME

Number	Name	Age years	Sex	Duration of hospitalization	Associated physical disease	Reaction			Complications and side effects
						Excellent	Good	Poor	
1	N.Z.	75	M	13 mos.	Arteriosclerotic heart disease			X	Confusion, tremors
2	P.W.	66	M	16 mos.	Parkinson's disease			X	Tremors
3	S.S.	70	M	27 mos.	C.V.A., diabetes			X	Confusion
4	A.S.	61	M	126 mos.	Parkinson's disease			X	Increased agitation
5	C.S.	80	F	16 mos.	Neoplasm, congestive heart failure			X	Increased confusion
6	F.S.	84	F	8 mos.	Congestive heart failure			X	Increased confusion
7	N.R.	59	M	14 mos.	Parkinson's dis., heart disease			X	Increased confusion
8	P.P.	59	F	47 mos.	Rheumatoid arthritis			X	Nil
9	R.M.	78	F	15 mos.	Bilateral hip fracture			X	Vertigo
10	E.M.	43	F	15 mos.	Schilder's disease			X	Nil
11	R.K.	85	F	62 mos.	Hip fracture			X	Nil
12	B.K.	67	F	42 mos.	Parkinson's disease			X	Drug rash
13	C.G.	86	F	12 mos.	Parotid tumour			X	Increased confusion
14	H.B.	78	M	155 mos.	Diabetes, bil. amp.			X	Increased confusion
15	D.A.	74	F	8 mos.	Hemiplegia			X	Increased confusion
16	A.T.	73	F	109 mos.	Right heart failure		X		Nil
17	D.G.	76	M	79 mos.	Diabetes, amputation			X	Increased confusion
18	M.S.	63	F	17 mos.	Ca. bile duct, heart disease		X		Nil
19	S.N.	67	F	28 mos.	Hypertension, C.V.A.		X		Nil

TABLE III.—DEPRESSIVE REACTIONS

Number	Name	Age years	Sex	Duration of hospitalization	Associated physical disease	Reaction			Complications and side effects
						Excellent	Good	Poor	
1	T.S.	63	F	17 mos.	Multiple sclerosis		X		Nil
2	L.A.	53	F	22 mos.	Multiple sclerosis			X	More disturbed
3	I.S.	60	F	109 mos.	Anemia	X			Nil
4	E.G.	59	F	6 mos.	Hemiplegia	X			Nil
5	E.D.	58	F	29 mos.	Multiple sclerosis	X			Nil
6	I.B.	68	F	3 mos.	Fracture hip	X			Nil
7	M.H.	60	F	66 mos.	CO poisoning	X			Nil
8	L.M.	30	F	52 mos.	Cerebral palsy	X			Nil
9	N.M.	25	F	62 mos.	Hemiparesis		X		Nil
10	J.B.	51	M	66 mos.	Rheumatic heart disease, Hemiplegia	X			Nil
11	S.I.	73	M	15 mos.	Diabetes, gangrene			X	More paranoid
12	R.A.	82	F	4 mos.	Rheumatoid arthritis	X			Nil
13	F.K.	50	F	4 mos.	Ca. breast with metastases			X	Deceased
14	R.L.	39	M	27 mos.	Multiple sclerosis		X		Nil
15	R.M.	70	F	16 mos.	Diabetes, heart failure			X	Nil
16	B.K.	69	F	8 mos.	Rheumatoid arthritis			X	Edema
17	R.N.	32	F	2 mos.	Multiple sclerosis			X	Blurred vision

Tables I, II and III summarize the basic data on each patient. These include the age and sex of the patients, the duration of hospitalization at the time of the drug study, and the primary associated physical disease. The clinical response to the drug is described as "excellent", "good" and "poor", the terms being used with the usual connotations and meanings found in comparable drug studies. Complications and side effects are also noted. Table V records some selected and illustrative changes recorded in the laboratory data from these patients.

Table I summarizes the clinical findings in a group of eight patients who suffered primarily from Parkinson's disease. The average age in the group is 67 years; the duration of hospitalization varies from five months at one extreme to 216 months at the other. Two patients manifested an appreciable response to administration of tranylcypromine with trifluoperazine, one described as excellent, the other as good. In this group of eight, six patients had side effects. A generalized morbilliform drug rash in one patient appeared on the fifth day and cleared when the drug was stopped. Two patients displayed increased confusion, and one patient, increased frequency of seizures. It is uncertain whether such changes were in fact produced by administration of tranylcypromine with trifluoperazine or because of discontinuation of the previously administered anti-parkinsonian medication.

Table II summarizes the results in a series of 19 patients who presented with features of the chronic brain syndrome. The usual and typical clinical findings were confusion, disorientation and memory impairment, which could be related to a variety of underlying types of cerebral pathology. The average age in this group was 71 years. A variety of associated organic diseases were also noted in addition to the primary diagnosis. Only three patients in the group of 19 definitely improved with administration of tranylcypromine with trifluoperazine. Among the side effects, one patient had a drug rash, one had vertigo and nine others were more confused.

Table III includes 17 patients with depressive reactions in addition to their physical disease state. The average age of this group is 55 years; however, this gives a rather deceptive impression since the inclusion of four patients aged 25, 30, 32 and 39 years noticeably lowered the mean age of the group. Another feature of this particular group is the relatively shorter length of hospital stay at the time of the drug trial. Eight patients showed an excellent response and three others were markedly improved. This was reflected by a brightened affect, the disappearance of depressed feelings and symptoms, improved co-operation, increase in activity, improved appetite and socialization, and emergence from their previously regressed state. Improvement here was sharp, unmistakable, and could not be related to spontaneous recovery. An imipramine study and others of a similar order had previously been carried out under similar conditions without any apparent effect.

Among those with side effects in this group were one patient with increase of edema, one with blurring of vision and two patients who became mentally worse, that is, more paranoid and disturbed. One patient died. This was a patient with cancer of the breast and extensive metastases. The drug was given to this patient in the hope that more effective pain control might result. However, no particular benefits were noted. The death was a typical "cancer death", and was not related to the drug administration in the opinion of the physicians who carefully reviewed all the data on this case.

TABLE IV.—SUMMARY OF CASES

Diagnosis	*No. of cases*	*No. improved*	*No. with side effects*
Parkinson's disease.....	8	2	6
Chronic brain syndrome...	19	3	13
Depressive reactions.....	17	11	4
	44	16	23

Table IV summarizes in brief form the total number of cases by diagnosis and the number improved. In this study, 16 of 44 patients are recorded as showing a good to excellent response. This is reported as a noteworthy effect, considering the type of patient concerned, and bearing in mind the previously disappointing experiences with other drugs. Side effects are recorded in approximately 50% of this series, and these will be described in more detail.

Table V records some of the laboratory data. The hemogram completed before and after the drug trial for each patient included estimations of the hemoglobin, erythrocyte count, colour index, leukocyte count, sedimentation rate, hematocrit and differential leukocyte count. No special change in any of these estimations was noted in association with the administration of tranylcypromine with trifluoperazine. The leukocyte count remained unaffected during drug administration. An interesting finding was the frequent elevation of non-protein nitrogen (NPN) levels after the drug trial. Actually this elevation did not reach pathological levels, but a rise was nevertheless recorded in no fewer than 37 of the 44 patients. This suggests that renal excretion is the main channel for elimination of this drug from the body. This finding suggests the need for special caution in patients with renal disease. Another possibility is that the NPN changes noted reflect decreased renal blood flow associated with a degree of hypotension. Urinalysis in all patients showed no abnormality in frequent tests. The alkaline phosphatase activity was slightly increased or decreased after the drug was administered, but these changes were so minor as to be of little significance. Blood pressure readings

TABLE V.—LABORATORY DATA

Number and name	*Hemogram*	*Urinalysis*	*NPN (mg.%)*	*Alk. phosphatase*	*B.P. changes*
2. R.A.	Leukocytosis	No change	Before 26.0 After 32.5	4.0 units 5.0 "	Decreased
8. H.B.	No change	No change	Before 23.0 After 33.5	7.5 " 5.8 "	Nil
17. B.K.	No change	No change	Before 23.0 After 33.0	8.3 " 8.8 "	Nil
37. S.S.	No change	No change	Before 25.0 After 45.0	12.6 " 5.8 "	Nil
43. M.Z.	No change	No change	Before 19.0 After 36.5	13.0 " 9.75 "	Nil

were carefully charted. Fifteen of the 44 patients developed definite hypotension, the average blood pressure decrease being of the order of 20%. This calls attention to the fact that hypotensive effects may appear as side effects and should be watched for. There may possibly be some place for tranylcypromine with trifluoperazine as a hypotensive agent in the treatment of some cases of hypertension. The side effects of hypotension may be listed as weakness, vertigo and increased confusion due to cerebral anoxia.

The side effects recorded in the patients in this series were not serious and were felt to be evidence of the introduction of a potent drug. Evaluation of these effects is complicated by the fact that Parstelin is a combination of two drugs, and it is sometimes difficult to know which of the two is responsible for the undesirable side effects. No complications of a serious or irreversible nature occurred in this series of seriously ill aged people who are presumably more vulnerable to the ill effects of pharmaceutical agents than are other patient groups. Two patients, as noted, developed a drug rash which cleared when the drug was withdrawn. Two patients developed an increase of edema. One patient had more frequent seizures and fourteen seemed more confused, disturbed or weak while on the drug. This could well be associated with the hypotension and/or withdrawal of other drugs which had been taken for a long time in certain cases. In a younger patient group of much larger size the paucity of side effects is one of the special virtues of this particular antidepressant medication.[9]

DISCUSSION

Tranylcypromine with trifluoperazine (Parstelin) is an antidepressant agent of considerable promise. The clinical effects were evidenced within a matter of two to three weeks in this group of chronically ill patients. While it was noted that the more aged patients did not do as well as the younger group, the response in certain patients was a definite and marked improvement that could hardly be explained on the basis of chance. The most striking effectiveness of the drug preparation was noted in those patients with depressive reactions. The presence of associated organic disease does not eliminate the likelihood of improvement in these cases, as all of these patients were severely ill and were admitted to hospital for the treatment of the physical disease state rather than for management of the depressive reaction. An agent of this sort is a most welcome therapeutic addition, as it can be used to relieve not only the obvious and manifest depression but also the concealed or latent affective disorder which so often accompanies chronic illness. In spite of the high incidence of side effects in this series, there were no serious complications, and there exists a wide margin of safety in the dosages described. In fact, we know of no absolute contraindications to its use, but note the possible need for special caution in patients with renal disease.

SUMMARY

Tranylcypromine with trifluoperazine (Parstelin), a potent antidepressant, was given to 44 chronically ill hospitalized patients, most of them aged. Sixteen patients were markedly improved, 11 of these in a group of 17 depressed patients. In this latter group the improvement rate was 65%, a striking response in patients who have associated chronic disabling disease. Although side effects were frequent (50% of the cases), no irreversible complications were observed.

Tranylcypromine with trifluoperazine is estimated to be a preparation of value in this type of patient for the relief of depressive symptoms, and merits further trial and evaluation.

Smith, Kline & French provided Parstelin for this clinical trial, and assisted with funds for the laboratory work.

Thanks are expressed to Drs. E. Roth, F. Newby-Good and I. Zador, Nursing Sister Mrs. L. Wright, and other personnel who assisted in this study.

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SPECIAL ARTICLE

RESEARCH AND TEACHING OPPORTUNITIES IN A UNIVERSITY-CENTRED CHILD HEALTH PROGRAM*

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THE 1959 Report on Medical Education in the United States and Canada by the Council on Medical Education and Hospitals of the American Medical Association[1] made some very pertinent observations concerning the role of research in teaching. It urged that research be viewed in its proper perspective in the total teaching program of the medical school. It emphasized that research is but one of the components of good teaching and that it should be used to develop those attributes in the future physician that we deem to be essential. Among these are critical intelligence, imaginative curiosity, controlled compassion, and a persistent will to find solutions to problems. As an ideal, research should be used to complement and strengthen rather than to compete with or even to replace some of the older and more traditional components of the curriculum. A word of warning has been given by Long.[2] The relatively easy accessibility of funds for research makes overemphasis an ever-present potential danger. If we are to have good medical schools and good universities, he feels that it is essential to have staff members who are not only competent investigators but also capable of transmitting knowledge to the next generation. It has become apparent over the years that research activity is an integral part of a well-rounded medical education. Our real problem is how to co-ordinate and integrate properly this student research into the total educational process.

A recent editorial in the *Canadian Medical Association Journal*[3] makes some interesting comments concerning this report. In its opinion, research and medical education touch at two points. Exposure of medical students to some research during their undergraduate days may be helpful in cultivating a proper critical attitude to their future life work. A limited contact with laboratory and experimental methods should sharpen the student's wits and prepare him for an attitude of suspicion toward dogma and empiricism. It may help him to realize the fallibility of many laboratory methods and, perhaps, to exercise more discrimination in accepting laboratory diagnoses as gospel. The second point is that medical research is of value only when its results can be communicated to the practitioner of medicine. The rift apparently growing between the medical research worker and the practitioner of medicine can, possibly, be narrowed if our future practitioners are trained in research as undergraduates.

This paper will deal with the development of student research as an integral part of the undergraduate curriculum in the Faculty of Medicine at the University of British Columbia. It will tend to concentrate upon the research activities of the Department of Preventive Medicine and, in particular, upon its newly developed Child Health Program. The Child Health Program will serve to illustrate not only how student research and teaching may be integrated but also how the clinical and preventive aspects of health care may be developed on an interdepartmental basis. Its origin, development and activities are visible signs of our recognition of the changing pattern of medical practice and our attempt to cope with new problems.

The medical school at the University of British Columbia is a young school in a rapidly growing university. The first class in medicine began its studies in 1950. At the outset, we realized that we had an obligation to teach much more than the basic elements of clinical medicine. We knew that we must attempt to implant the scientific attitude and excite the intellectual curiosity of our students so that they would be motivated to continue the learning process throughout their entire professional lives. The most recent evidence of our adherence to this philosophy has been the creation of a full Department of Continuing Medical Education. From the beginning, we believed that exposure to and training in the elements of medical research would be one realistic approach to the attainment of our objective.

Many medical schools have introduced research as a part of their curricula in recent years. They have done this for a variety of reasons and have approached it in a number of ways. At U.B.C. there were good grounds for our thought that student medical research was an important part of undergraduate education. In Canada we have a rich heritage in medical research from such men as Banting, Best and Selye. We have the example of the great teacher, Sir William Osler, who in his long and distinguished career stimulated the enquiring minds of a host of medical students in Canada, the United States and Great Britain. We knew that great contributions to medical knowledge had been made by undergraduate medical students. These have been beautifully recorded by Gibson[4]

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*From the Faculty of Medicine, University of British Columbia, Vancouver 8, B.C. Presented at the meeting of the Association of Teachers of Preventive Medicine, San Francisco, California, October 30, 1960.

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in his recent book. We were impressed with the fact that some of the most significant advances in medicine have come from physicians whose primary field of activity was not medical research. Family physicians from Jenner to Pickles have, through keen observation, made great contributions while engaged in busy clinical practices.[5] Concerning the latter, Paul,[6] quoting Greenwood, makes a plea for the recognition of the value of the "amateur" in research. We felt that wherever our students might go after graduation, whatever fields of medicine they might enter, the opportunities for research would be present. A certain few of our graduates may make a career of medical research. However, we thought it important that all of our students should have training so that they might recognize and take advantage of opportunities for research wherever they occur in the future.

It soon became obvious that if we expected our students to have an appreciation of the importance of research, we had to give them certain training. They had to have time, opportunity and guidance in carrying out original research as an integral part of their undergraduate education. This has involved a continuous process of curriculum modification to the point where all of our students now carry out research activities. Thus, it would seem worth while to outline its history with particular reference to the Department of Preventive Medicine.

THE THESIS FOR GRADUATION

A satisfactory thesis is a prerequisite to graduation in the medical school of the University of British Columbia. We realize that we are one of a very small number which make this a requirement. Two reports have been published on the experience of Yale University where, with the exception of two brief periods, the thesis has been a requirement since 1839.[7, 8] There, the thesis is compulsory and must be based upon original research. Generous time is provided throughout the course for this activity. At Yale the thesis is felt to be important since it gives students the opportunity to explore critically the literature in a limited field, to bring an investigation to a conclusion, to write a report, to know the strengths and limitations of biological research, to have curiosity stimulated and to work intimately with the faculty. At Yale they believe that it will enhance the competence of the future physician and make him a better citizen of the medical world. They have attempted to evaluate the results even though they acknowledge the inherent difficulties. In comparison with other medical schools, a high percentage of Yale graduates are certified by the Specialty Boards,[9] and many of them have entered careers in academic medicine and research.[10] They do not suggest that student research is the sole factor responsible but do consider that it has a bearing.

Our approach to the thesis has been somewhat different. It is a prerequisite but it does not necessarily embody original research. It may be the result of original investigation or may be a planned course of study in a field of learning related to medicine. The subject of the second-year research project, which was inaugurated in 1957 and which will be described subsequently, may be expanded as the theme for the thesis. We believe that the preparation of the thesis is a valuable part of the student's education. It gives him familiarity with medical literature and the proper use of the library. He is being prepared to deal adequately with future publications because of the experience he has gained. In addition, in most cases, it has a direct applicability to research since the vast majority of the theses deal with original investigation. By the middle of his third year the student selects a topic for his thesis. He consults with a member of the faculty who, after thorough discussion, agrees to act as his sponsor and mentor. The sponsor arranges for facilities in departmental space or in co-operating hospitals and health departments. He helps the student to plan his research, supervises its progress and assists in the development of the thesis. The standard of quality that may be achieved in such reports is manifested in the thesis of a recent medical graduate which has since been published as a series of articles in this journal.[12]

SUMMER EMPLOYMENT OF MEDICAL STUDENTS

As a department, we became involved in student research very early. Primarily, this was possible because of an unusually close relationship with the British Columbia Department of Health. Since 1952 we have been able to offer summer employment to a selected group of students. The original purpose of this summer employment was to render aid to local health agencies. However, from the beginning, it was agreed that the students would also be assigned research projects under the direction of this department. Wherever possible, students are employed for two successive summers so that the research project may be fully developed. A number of students have used these periods of summer employment to obtain material for their theses and have published several good papers.

The number of students employed and their activities have varied from year to year, but the past summer illustrates well the research potentialities and the wide range of interests involved. Eight students were employed, five of these being in major research projects within the Department of Preventive Medicine and three in local health agencies. The research projects within the department were co-operative efforts with various community agencies. Three students were involved in a study of the pattern of hospital utilization in this area. This is a study involving the Provincial Government, the medical profession and the University. Its findings will have a direct bearing upon future hospital construction. Another student was engaged in a study of the factors involved in pedestrian traffic accidents in children. This was

centred in our Child Health Program and involved many community agencies. The fifth student was engaged in the development of an experimental camp for handicapped children which will serve as a model for expansion in the province as a whole. This experimental camp was under the direction of the Child Health Program. Three students were employed in local health agencies. One of these students has studied two vexing problems in venereal disease—primary syphilis among male homosexuals and non-gonococcal urethritis. The second student has been concerned with a study of the control of enteritis in a large residential institution for mentally retarded children. The final student worked with the Provincial Division of Tuberculosis Control on an evaluation of therapy of pulmonary tuberculosis carried out on an outpatient basis. All of these internships have been financed through National Health Grants. They have given the students valuable research experience, they have been of great help to health agencies, and the findings from these studies will be of value far beyond the local scene.

SECOND-YEAR RESEARCH PROJECTS

In the first few years of existence of U.B.C.'s medical school, student research was a departmental responsibility and no specified time was provided in the curriculum. It soon became apparent that it had to be placed on a more formalized basis and free time had to be provided. Accordingly, in 1957, one day each week was made available for student research projects in the second year of the medical course. Now, all students are required to participate in research as a part of their undergraduate training. Each year, the Department Heads submit to the Dean a list of student research propects which they are willing to sponsor. These lists are made available to the students at the beginning of the first term. Sufficient projects are available so that the students have a relatively wide choice of subject. The student picks the project upon which he would like to work. Facilities for the project are made available within the departments where the work of the student must be supervised by a faculty member to whom a report is submitted before the end of the second term. Satisfactory performance is required for promotion of the student. As has been noted, a number of students expand these second-year research projects into their theses for graduation. The reaction to and performance in these research projects cover a wide range. Some students are keenly interested, work long hours beyond the specified time and produce creditable results. Others passively accept the research project as a requirement and give it only the time and effort that they must. A few have to be urged, cajoled and even pressed into giving an acceptable minimal performance. However, we are convinced that the effort is worth while, that the time assigned in the curriculum is justified and that research is definitely a part of the training process of the medical student.

THE CHILD HEALTH PROGRAM

A number of these student research projects have been centred in our Child Health Program, and a description of these will serve to illustrate the pattern in the medical school as a whole.

We feel that our Child Health Program has certain unique features, and a description of its origin, development, scope and purposes may be of interest. A preliminary report has already been published.[11] The Professor of Pediatrics, who is now the Dean of the Faculty of Medicine, and the Professor of Preventive Medicine had planned toward a campus-centred Child Health Program for a number of years. We had not been satisfied with having the entire teaching of pediatrics in the hospital atmosphere among sick children. This traditional approach was obviously unsuited to the changing picture of child health care where the practitioner spends more of his time with the problems of the apparently well child than with the acutely ill as he did in the past. We were keen to integrate much more closely the preventive and therapeutic aspects of child care because we are of the firm opinion that preventive medicine is best taught in conjunction with clinical instruction. We did not feel that this teaching could be done in a Health Department facility such as a traditional Well Baby Clinic, since these must, of necessity, be service-oriented and teaching and research would assume secondary roles. The ideal situation we felt would be to have a large group of normal children under our direct supervision where teaching and research could be carried out on a controlled basis.

The opportunity to inaugurate this venture came with the appointment of a new staff member (J.H.R.) who was qualified in both preventive medicine and pediatrics and who received academic appointments in both of these departments. The program got under way at the beginning of 1959.

A suitable group of children was easy to find. The approximately 11,000 full-time students at the University of British Columbia have more than 1200 children. Most of these are in the infant and preschool age groups. More than half of these families are housed on or in close proximity to the campus. Like students everywhere, they are in a low income group and are most interested in cutting their expenses wherever possible. The University administration was eager to have this service rendered to the students, and the local medical profession was quite willing for the University to assume this service role. Other faculties and schools in the University, as well, were in favour of the development of this new facility. Finally, health authorities at local, provincial and federal levels were most enthusiastic about the plan, and assurance of financial support was provided.

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The Child Health Program is housed on the campus close to the Department of Preventive Medicine and at some distance from the teaching hospitals. Physical facilities are ideal and a team of physician, nurse and social worker has been established. We have now had nearly two years of experience with this venture and are satisfied that it fills a real need in the University community. It provides facilities for teaching and research which are unique, allowing us to integrate the teaching of pediatrics and preventive medicine in a realistic approach to current problems in child care.

Our basic objectives were in the areas of teaching and research but we fulfil a service role as well. These children receive all the components of a complete well-child service, free of charge and on an appointment basis. There is a leisurely and personalized atmosphere. When a child is received into the program, the parent is told in detail of the teaching and research aspects and agrees to the child's being used for these purposes. The student parents have received the service with enthusiasm; they appear to enjoy the atmosphere of teaching and research and they are most appreciative of the excellent care received. No difficulty has arisen in obtaining an ample number of infants and children for our purposes. The child with illness is referred to his family physician or pediatrician, who has been most co-operative.

Teaching, in the main, has been confined to second-year medical students. All of the basic teaching in pediatrics—history taking, physical examination, growth and development—is centred in the Child Health Program. In addition, there is a very easy integration with the teaching of the preventive aspects of child care such as immunization, accident and poison control, and the progression onwards into school health and care of handicapped children is readily accomplished. We have just begun to extend our teaching into other schools and faculties, and our facilities are being increasingly utilized by public health nurses, social workers, psychologists and teachers in training. Already, we have entered into the field of graduate medical training. Assistant residents in pediatrics from certain of the city hospitals are rotated through the program for periods of two months each. We are convinced that the Child Health Program offers excellent teaching facilities for both pediatrics and preventive medicine.

Research activities are developing satisfactorily both in the graduate and undergraduate areas. It has been mentioned that one of our students was employed last summer in a research project concerned with the investigation of factors involved in pedestrian traffic accidents in children. This is under the direction of a full-time health officer who has been assigned to us by the province for a year. He will receive credit for this year in his specialist training program directed towards his certification by The Royal College of Physicians and Surgeons of Canada. Several of the research projects as required in the second year of the medical course have been conducted in the Child Health Program. A brief description of two of these will serve to illustrate its research potentialities.

A number of new features were incorporated into the design of the equipment of the Child Health Program in an attempt to improve the ease and quality of the examination of children. For example, two of the examining tables were built eight inches lower than usual, with a central knee space. These are used for infants with the mother and the physician comfortably seated on either side with the baby between them. This allows a relaxed, informal atmosphere and the physical and developmental examination is greatly enhanced. The design of equipment was kept simple and practical with the objective in mind that the practising physician could use similar types in his own office.

Ceiling mirrors were installed above all the examining tables. It was felt that mirrors would help to keep children occupied during the examination and would serve as a useful distraction for two- and three-year-old children who often show resistance to lying back on the table. Our experience with the mirrors was as we expected, but there did appear to be occasional unfavourable fear reactions and, in the very young infant, the mirror seemingly failed to catch or hold his attention. One of our second-year students chose as his research project the evaluation of the ceiling mirror as an aid in examining children. Controlled conditions were achieved by using a device to block out the mirror as desired. Seventy children were studied, ranging in age from one month to five and one-half years, with nearly 80% less than two years of age. With about 40% the mirror was definitely useful; with a further 17% it had minimal usefulness; with about 41% it appeared to serve no useful purpose; and in only one child was there an adverse fear reaction. This was a child in whom other psychological difficulties had already been noted. The mirror seems to be most useful in overcoming the reluctance of the child to lie down on the table. It helps in abdominal relaxation and, in very young children, is of help in examination of the ocular fundi. This study was admittedly incomplete but it did reinforce our belief that the mirror has value and the student's findings gave us useful leads for further investigation.

After a year of operation of the Child Health Program we were very keen to attempt an evaluation of parental reaction. A medical student assumed this study as his second-year research project, since he was particularly interested in improving his interviewing techniques. The student carried out home visits to 60 families who represented 23.6% of those registered. The reaction of the parents to the service rendered was gratifyingly enthusiastic. Questions were asked relative to the teaching and research activities. Any criticism made by the parents was of a constructive nature and will

result in a number of minor modifications. We are reassured that no real difficulties exist. This was a most useful study because it gave us not only a gauge of the reaction of parents but also a guide for our future activities.

A number of student research projects within the Child Health Program for this academic year are now under way. Among these are evaluation of growth charts, study of hip abduction and longitudinal studies of personality development. There are literally dozens of areas of investigation we would like to pursue. Our chief limitations are with regard to staff time for supervision. We visualize these student research projects as being of great mutual benefit not only to the student but also to the proper development of the program as well.

SUMMARY

The development of student research in the Faculty of Medicine at the University of British Columbia has been presented as an integral and required portion of the undergraduate curriculum. Special attention has been paid to student research activities within the Department of Preventive Medicine and, in particular, in its Child Health Program.

Because we are firmly convinced that research is an essential part of the proper training of all physicians, we believe that student research should be a required activity in the curriculum. If viewed in its proper perspective, it can be used to strengthen other aspects of the total teaching program. Its implementation and its apparent objectives may vary from school to school but its end result will be the same—a better-trained physician who will be better fitted to make his maximal contribution to society.

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CASE REPORTS

MALIGNANT GANGLIONEUROMA: REPORT OF A CASE OF AN AGGRESSIVELY GROWING IMMATURE GANGLIONEUROMA*

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GANGLIONEUROMAS are relatively uncommon tumours. Stout[6, 7] has divided them into two groups as follows: (a) Differentiated ganglioneuroma, an encapsulated tumour composed of fully differentiated ganglion cells set in a dense background of sheath neurites, and (b) partially differentiated ganglioneuroma; this is an incompletely differentiated tumour, as its name implies. The latter has two principal variations — one composed of a mixture of areas of complete differentiation and immaturity, the other a relatively uniform tumour of ganglionic elements showing more or less the same degree of immaturity. The term "immature" ganglioneuroma has also been used for this second type (Horn, Koop and Kiesewetter[2]). Approximately one-fourth of the entire group of ganglioneuromas can be classified as immature or incompletely differentiated.

The case to be reported is an example of the partially differentiated or immature ganglioneuroma growing in what has been described as "hourglass" or "dumbbell" fashion in relationship to the spine. This growth pattern is characterized by paravertebral, intraforaminal and intraspinal involvement, and produces the neurological changes of spinal cord compression. In 1958 Shephard and Sutton[5] reported four cases of "dumbbell" ganglioneuromas involving the spine. In reviewing the literature they found only 11 additional cases. On the basis of the clinical features of these 15 cases the authors suggested that a more radical policy toward treatment might be appropriate, especially in children, before persistent neurological damage is produced. The importance of this implication may be seen in our case, although it is overshadowed by the massive presence of invasion, especially of the lungs. In 1960 Oberman and Abell[3] added five more cases of "dumbbell" ganglioneuroma. It seems likely that this growth pattern may be more common than the reports in the literature indicate.

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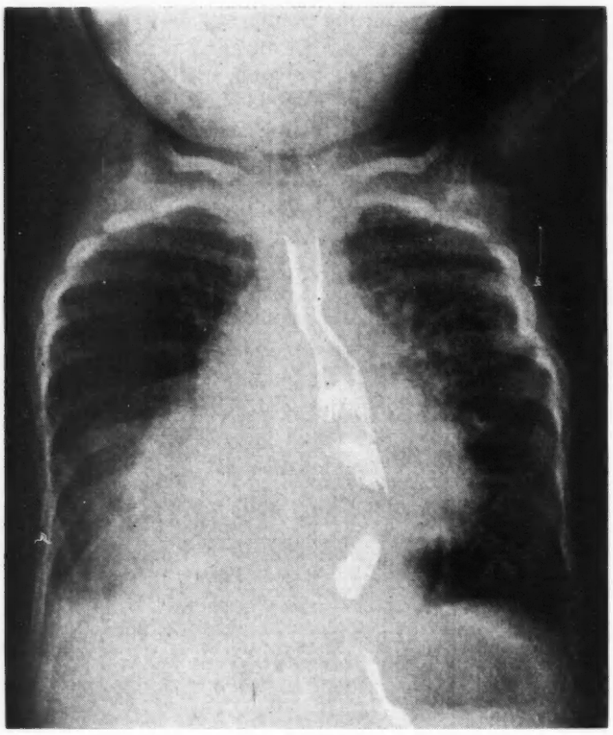

Fig. 1(a)

Fig. 1(a).—Anteroposterior roentgenogram of chest, after barium meal, showing soft tissue mass in right hemithorax, nodular involvement of mediastinum and displacement of the esophagus anteriorly and to the left (two weeks before death).

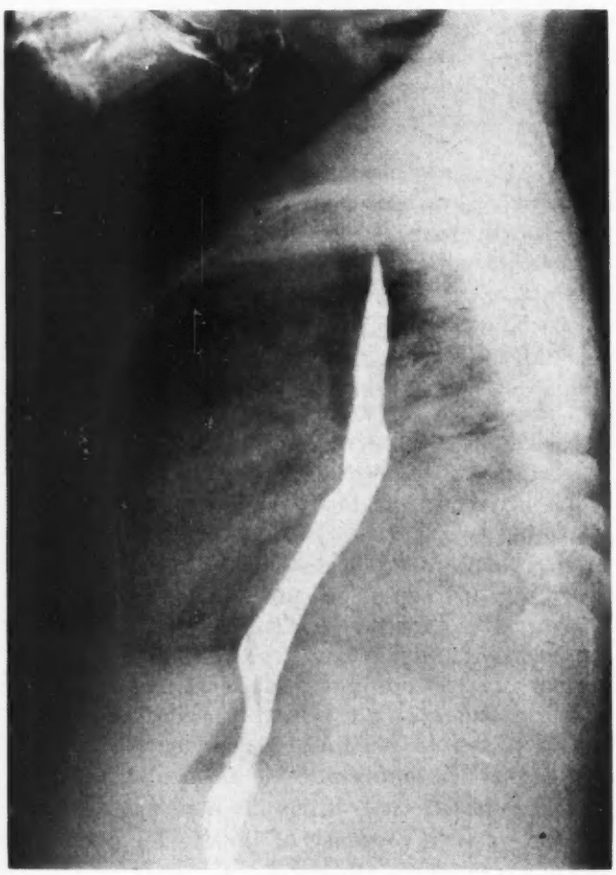

Fig. 1(b)

Fig. 1b.—Lateral roentgenogram of chest, after barium meal, showing soft tissue mass in right hemithorax, nodular involvement of mediastinum and displacement of the esophagus anteriorly and to the left (two weeks before death).

The patient, a 3-year-old white girl, had an uneventful delivery but soon developed respiratory distress and cyanosis. At the age of eight days she was admitted to the Henry Ford Hospital. Studies led to a diagnosis of Eisenmenger's complex with hypoplasia of the aortic arch and patent ductus arteriosus. At the age of 2 weeks she was operated upon for correction of the latter. Operation disclosed the additional finding of a mild coarctation of the aorta, but this was not considered to contribute to the cardiorespiratory symptoms. At this time there was no evidence of a mediastinal tumour.

Within the next two years it became evident that the coarctation was producing progressive impairment of circulatory and cardiac function. Chest roentgenograms now showed small amounts of fluid in both pleural cavities, left-sided cardiac enlargement and a density overlying the right lower lobe. There was also a deformity of the 12th rib on the right side and thinning of the pedicles of the 11th and 12th dorsal vertebrae, as well as a soft tissue mass in the right hemithorax posteriorly. There was a bulging mass, resilient and non-tender, measuring 14 x 4 cm., in the right side of the back. A myelogram revealed cerebrospinal fluid block at the level D 12 to L 1.

Biopsy of the tumour presenting in the back preceded repair of the coarctation. Posteriorly the tumour appeared well encapsulated, but at thoracotomy it was noted that there were nodular tumour implants overlying the aorta and that the tumour was invading diffusely about the root of the right lung. After repair of the coarctation, tumour tissue was removed from the lung root as cleanly as possible.

One month later thoracic laminectomy was performed and removal of the accessible portions of the intraspinal and paravertebral tumour was carried out. The tumour appeared to envelop the spinal cord almost completely. It was continuous with the extraspinal mass through at least two intervertebral foramina. Postoperatively there was leakage of spinal fluid through a small dural defect which necessitated closure four weeks later.

Progressive enlargement of the residual mediastinal tumour with massive infiltration of the right chest (Figs. 1a and 1b) led to another attempt at removal eight months later. The patient died on the operating table following cardiac arrest and failure of massage to resuscitate the heart.

Autopsy disclosed the entire mediastinum to be filled with nodular masses continuous with tumour in the right paravertebral region, extending from D 9 to L 2. The right lung was diffusely invaded by direct extension in an irregular nodular fashion (Fig. 2a). The tumour was uniformly rubbery and pale grey-pink. It had eroded the right 12th rib posteriorly, as well as the spine, and had invaded the spinal canal (Fig. 2b). The left lung and the other organs were free of tumour. The heart showed only mild generalized enlargement but moderate right ventricular hypertrophy. No evidence of coarctation was seen. The suture line of the former repair was still visible. The calibre of the thoracic aorta was mildly smaller than normal. Only slight congestion was evident in the internal organs. (Clinically, the remarkable improvement of her cardiac status had been recorded.)

Microscopic Examination

The tumour consisted of fairly well-defined, interwoven bundles of fibrils, interspersed with nests of

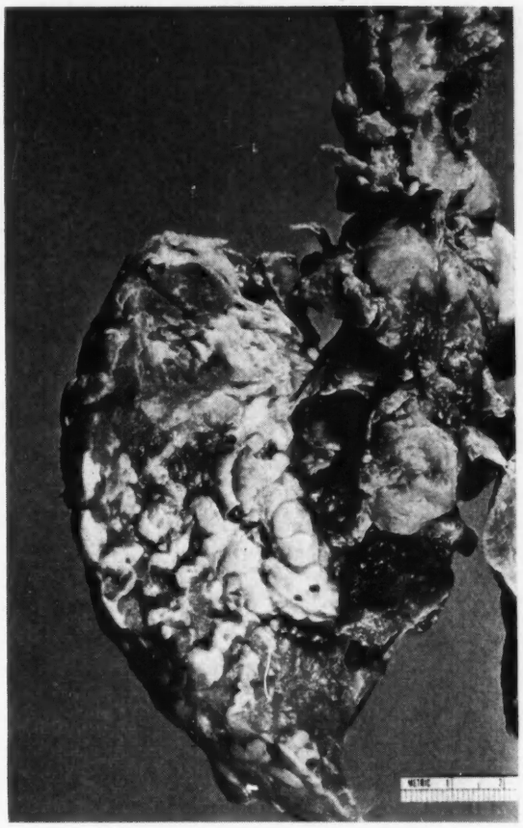

Fig. 2(a).—Photograph of sectioned surface of invaded right lung.

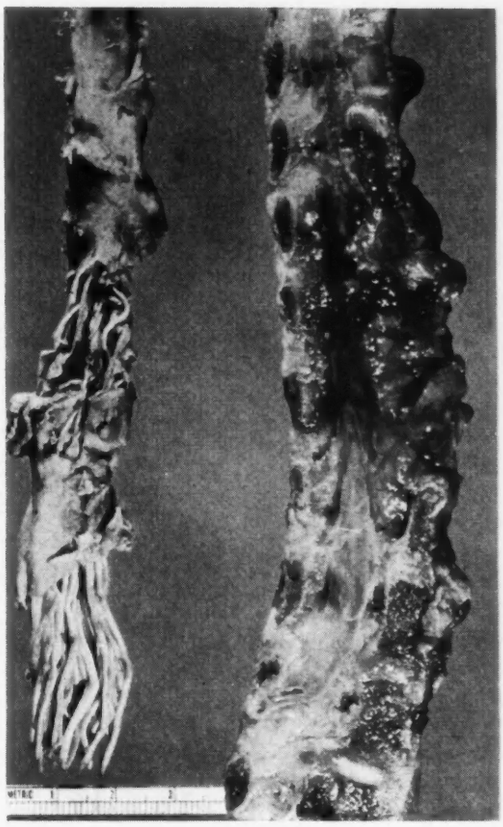

Fig. 2(b).—Photograph of invasion of low thoracic and upper lumbar vertebrae by tumour.

ganglion cells. In large areas the ganglion cells were completely mature but in other areas there was a diffuse admixture of mature and immature ganglion cells. As is usual with ganglioneuromas, the neurofibrillar stroma appeared to be excessively abundant as compared with the number of ganglion cells (Figs. 3 and 4a).

Scattered throughout were prominent aggregations of small round cells resembling lymphocytes. Only a few of these appeared to represent genuine lymphoid tissue with germinal follicles incorporated by the tumour. In the majority the cells seemed more pleomorphic than is consistent with lymphocytic or inflammatory cell infiltrate, and intimately intermixed with the small cells were recognizable immature ganglion cells and other larger cells with vesicular nuclei and prominent nucleoli (Figs. 4b, 5a and 5b).

The specimens obtained at the various surgical procedures and that examined at autopsy did not differ significantly in histological appearance. Nowhere was the tumour so undifferentiated as to suggest classification as neuroblastoma. All of the sections from the intraspinal tumour removed at laminectomy lacked the more immature cell forms and were uniformly well differentiated.

Because of the scattering of immature ganglion cells and larger cells with large vesicular nuclei and prominent nucleoli within the clusters of small round cells, it is believed that many, perhaps most, of these cellular aggregates represent examples of the "development centres" described by Scherer.[4] The presence of the varied cell forms within these clusters suggests transitions from the small cells to the immature ganglion cells and it is these transitions which, according to Scherer, distinguish the development centres from foci of lymphocytic infiltrate. Scherer actually describes two

Fig. 3.—Photomicrograph of the tumour invading the lung. × 70.

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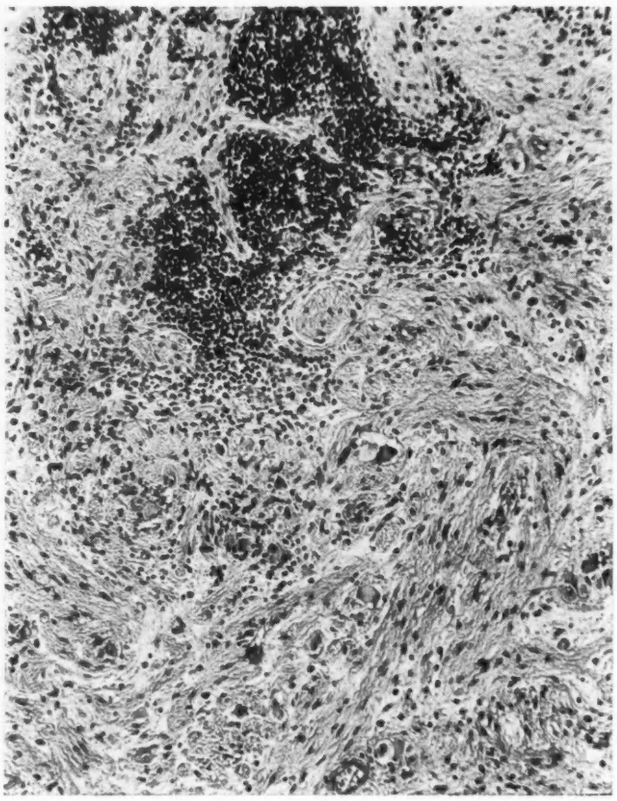

Fig. 4(a).—Focal collection of small round cells in the otherwise moderately well-differentiated ganglioneuroma. × 115.

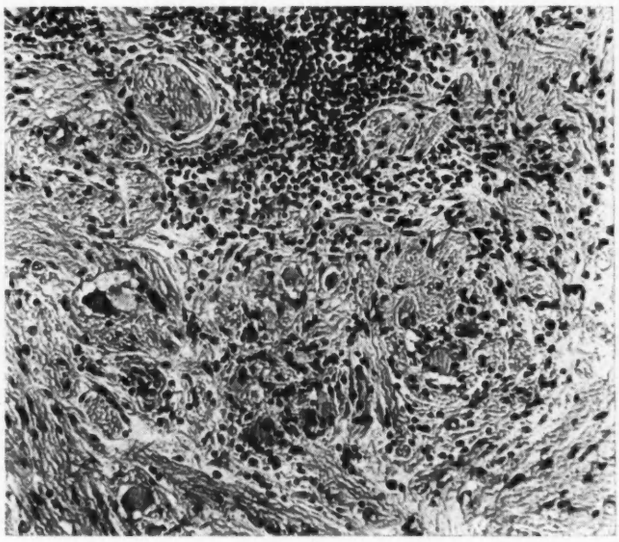

Fig. 4(b).—Ganglion cells of varying maturity are intermixed with the small round cells. × 250.

forms of development centre — one showing a continuous transition from sympathogonia to sympathoblast and immature ganglion cells, the other being represented by focal accumulations of cells exhibiting a more or less uniform degree of immaturity or maturity. If this degree happens to be at the level of sympathogonia, differentiation from lymphocytes may become extremely difficult, if not impossible, at least with routine histologic methods.

DISCUSSION

The unusually aggressive growth of the tumour in our case contradicts the general belief that the better differentiated tumours are less malignant in their clinical behaviour. In Horn, Koop and Kieswetter's series[2] of 41 children with neuroblastoma, 16 were alive without clinical evidence of disease at the time of his report. Eleven of the 16 survivors had been alive and well for at least four years since diagnosis and six had been followed up for periods ranging from 6 to 12 years. There was assurance of complete surgical excision of the tumour in only four of the 16 cases. Eighty per cent of the surviving patients showed fairly mature tumours, and conversely the great majority of the patients with more undifferentiated tumours died

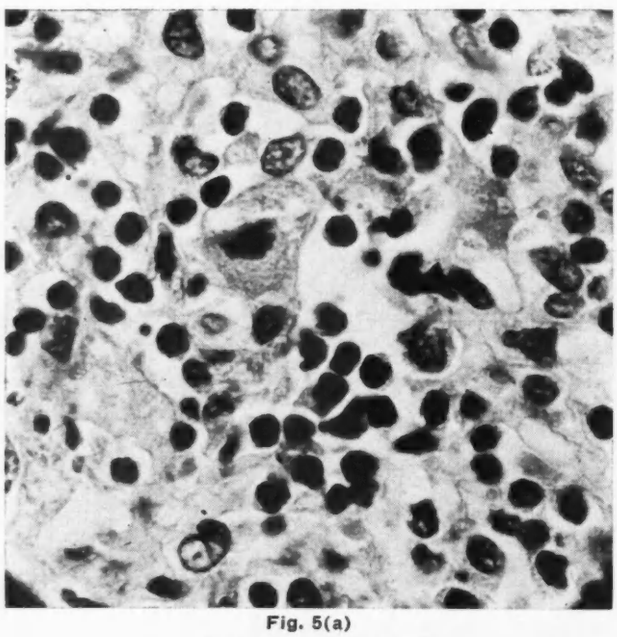

Fig. 5(a)

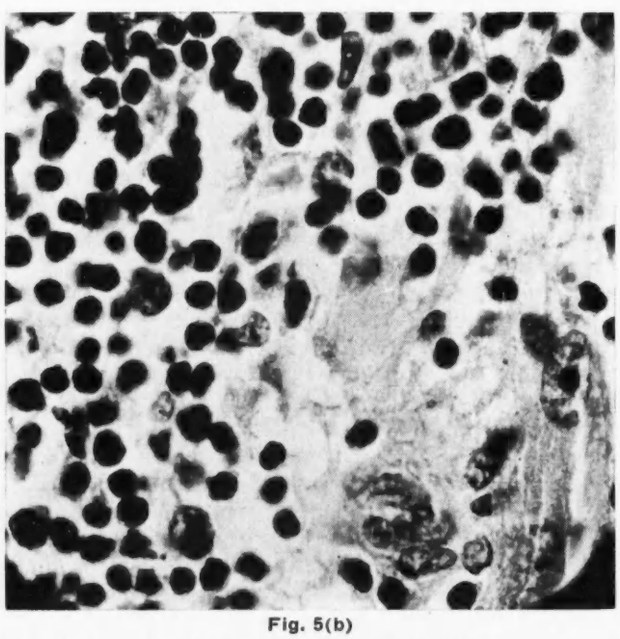

Fig. 5(b)

Fig. 5(a) and 5(b).—Higher magnification of central portion of Fig. 4(a) and 4(b) showing varying chromatin content of nuclei, occasional larger cells with vesicular nuclei and prominent nucleoli, and apparent transitions between the small round cells and the immature ganglion cells. × 1100.

in less than 14 months, although two survived. Horn concludes that a few children with neuroblastoma do survive despite dissemination.

Cushing and Wolbach[1] interpreted their widely quoted case as demonstrating progressive maturation from embryonal neuroblastoma to mature ganglioneuroma. Initial biopsy from the paraspinal portion of the dumbbell growth showed a neuroblastoma. Ten years later the extradural portion of the intraspinal tumour which was removed showed a well-differentiated ganglioneuroma. That this must be interpreted as progressive maturation is questionable in view of the fact that a certain proportion of these tumours show fields of maturity alternating with fields of immaturity, not to mention the fact that some children are known to survive despite the presence of an immature tumour. It is of interest that the case reported here parallels that of Cushing and Wolbach in that the tumour material obtained from the spinal canal showed the most advanced degree of maturation with an absence of immature forms.

Oberman and Abell[3] concluded from their series that there was no difference in clinical behaviour between mature and partially differentiated ganglioneuromas.

SUMMARY

A case of an aggressively growing immature ganglioneuroma in a 3-year-old white girl is reported. Despite large areas of advanced differentiation and absence of distinct neuroblastomatous features, the tumour proved to be highly malignant in so far as local growth is concerned. The fact that immature ganglioneuromas are on record that have pursued a considerably more benign course, indicates that the prognostic significance of the degree and extent of cellular differentiation is limited.

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ISOLATION OF SALMONELLA ORGANISMS FROM MESENTERIC LYMPH NODES

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Toronto

RECENTLY TWO unusual cases have come to our attention in which the patients underwent laparotomy with a preoperative diagnosis of "appendicitis"; however, at surgical exploration the picture was not obviously one of acute appendicitis. Enlarged mesenteric lymph nodes were noted and were removed. Bacteriological examination of nodes in both cases revealed the presence of Salmonella organisms. Because of this somewhat unusual finding, these cases were considered of interest and are reported in detail below.

CASE 1.—K.S., a 9-year-old boy, began to feel unwell on November 27, 1959, two days before admission to hospital, complaining of periumbilical pain which eventually shifted to the right lower quadrant of the abdomen. His temperature was 99° F. He had no history of vomiting but suffered from slight anorexia on the day of admission. Past illnesses included a cardiac operation at the age of three years (presumably for congenital heart disease) and a tonsillectomy on November 6, 1959. Physical examination revealed a young boy of athletic build. His head and neck appeared somewhat plethoric; there was no cyanosis. The conjunctivae were normal. Examination of the cardiovascular system revealed a systolic thrill over the apex of the heart. A systolic, grade three murmur was heard over the precordium and seemed to radiate all over the left chest. The blood pressure was 104/60 mm. Hg. The pulse was regular. The scar of his previous cardiac operation was noted. The lungs were clear to percussion and auscultation. The abdomen showed marked tenderness over McBurney's point. There was also evidence of rebound tenderness and general guarding of the abdominal muscles.

The leukocyte count was 10,500 per c.mm. Urinalysis was negative. Other investigations were not relevant.

A diagnosis of acute appendicitis was made and laparotomy was carried out. The appendix appeared to be in a state of mild early inflammation. Adjacent to the base of the appendix was an acutely inflamed mesenteric lymph node covered with fibrinous exudate. The inflamed node was shelled out and the point of removal was oversewn with catgut. The appendix was then removed in the usual manner.

The pathological appearance was as follows: Sections from the appendix showed that its lumen contained fecal material and mononuclear cells. All layers of the wall were intact, including the mucosa. There was some infiltration of the submucosa and muscle coat by scattered mononuclear cells and occasional eosinophils. The lymphoid tissue was quite prominent. A diagnosis of subchronic appendicitis was made.

The lymph node submitted to the laboratory was examined. The specimen consisted of a single piece of

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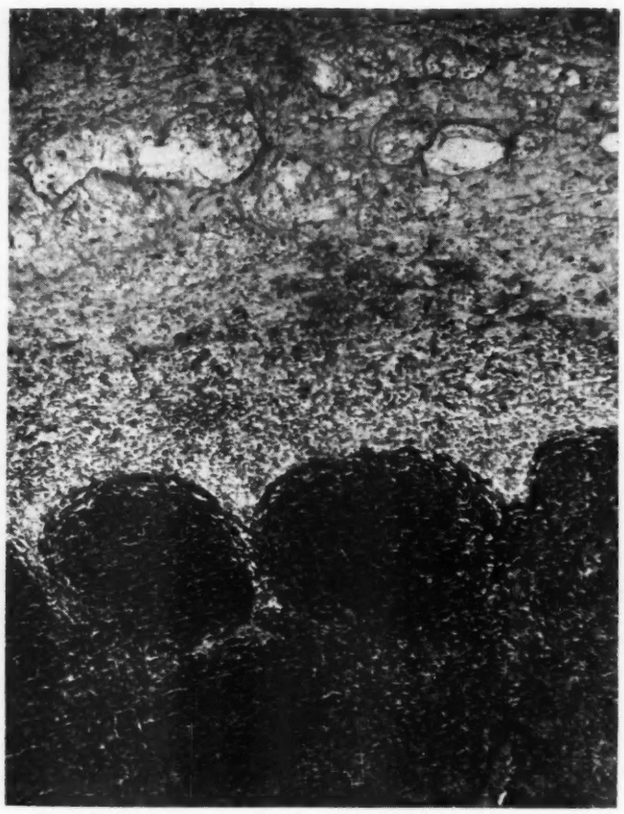

Fig. 1.—Mesenteric lymph node from K.S. showing inflammatory reaction in tissue surrounding node. H. & E., × 30.

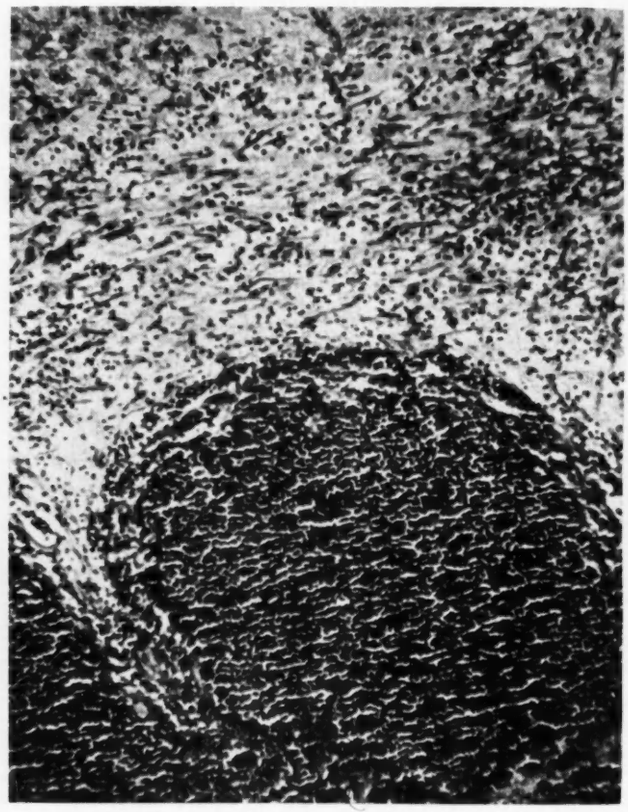

Fig. 2.—Higher magnification of Fig. 1. H. & E., × 120.

tissue containing a nodule, measuring approximately 1 cm. in diameter, and attached fibrofatty tissue, the whole measuring about 2 x 1 x 0.5 cm. The fibrofatty tissue appeared somewhat hemorrhagic. The nodule externally was tan-pink. On the cut surface it was cream-coloured and semitranslucent. Microscopically, the lymph node showed extensive evidence of reticulum cell hyperplasia. The adjacent fibrofatty tissue was heavily infiltrated by mononuclear cells, histiocytes, eosinophils and occasional polymorphonuclear leukocytes (Figs. 1 and 2). There were areas of extravasation of red blood cells in the tissue as well as of edema. On all sections examined there was no evidence of granuloma or malignancy. The pathological diagnosis was reticulum cell hyperplasia of the lymph node and subacute inflammatory reaction in the fibrofatty tissue surrounding it.

From the lymph node *Salmonella montevideo* was cultured.

Hospital course: Immediately postoperatively the child was placed on chloramphenicol therapy. He was discharged in good condition one week after admission to hospital.

CASE 2.—J.B., a 7-year-old boy, was admitted to hospital on January 15, 1960, with a history of nausea, headaches and recurrent abdominal pain for the previous three or four months. The history of past illness revealed that this child was well until approximately October 1959, when he began to suffer from vague abdominal pain, nausea, anorexia and frontal headaches. On one occasion he also had yellowish-white discharge from the right ear. There was no history of cough, sore throat, chest pain, vomiting, constipation, diarrhea, dysuria or any other complaints except for recent enuresis. The family history was noncontributory. Past illnesses were measles and chickenpox.

Physical examination showed a young boy in no apparent distress. The eyes, nose and throat appeared normal. The chest was clear to percussion and auscultation. Auscultation of the heart revealed a split second pulmonary sound, but no murmurs were heard. The cardiac rhythm was regular and the blood pressure was normal. No masses or organs could be palpated. The abdomen appeared flat. There was no tenderness or rigidity. The extremities were normal. There was no skin rash. Examination of the central nervous system showed no abnormal findings.

Laboratory findings included the following: hemoglobin value 10.5 g. %, leukocyte count 4900 per c.mm. with a differential count of metamyelocytes 6%, segmented neutrophils 60%, lymphocytes 30% and monocytes 4%. Urinalysis was normal, and porphobilinogen was absent. An intravenous pyelogram was negative.

It was felt that the condition was possibly due to appendiceal colic, and a laparotomy was performed. Through a right McBurney incision the peritoneal cavity was opened. The appendix was seen to contain several fecaliths and the mesenteric lymph nodes were markedly enlarged. A biopsy was taken from one of the lymph nodes and the appendix was removed in the usual manner.

The appendix measured 5.5 x 0.5 cm. The attached fat, measuring 0.2 cm. in maximum thickness, was unremarkable. The peritoneal surface was bluish-pink, smooth and slightly congested. On the cut surface the lumen was patent and filled with fecal material. The wall measured up to 0.1 cm. in thickness. Sections from the appendix showed that its lumen contained

fecal material. All layers of the wall were intact. The lymphoid tissue was somewhat prominent and showed some evidence of enlargement of the germinal centres. No pathological diagnosis was established as far as the appendix was concerned.

The pathological appearance of the lymph node was as follows: "The specimen consisted of a single piece of tissue measuring 1.2 x 0.6 x 0.35 cm. Externally it was pink with occasional hemorrhagic areas and moderately firm in consistency. The cut surface appeared similar. The microscopic examination showed a lymph node with reticulum cell hyperplasia. In some areas there was also evidence of enlargement of the germinal centres. In all sections examined there was no evidence of malignancy or other pathology. Diagnosis: Reticulum cell hyperplasia of lymph node."

Culture of the lymph node revealed the presence of a Salmonella organism identified by the Salmonella typing centre of the Ontario Department of Health as *Salmonella montevideo*. Subsequently, stool cultures were submitted and these grew *Salmonella tennessee*.

Hospital course: The patient was placed on chloramphenicol therapy and had an uneventful recovery, being discharged two weeks after admission to hospital. This patient's temperature during his hospital stay ranged up to 101° F. A Widal test failed to show evidence of agglutinating antibodies.

DISCUSSION

Cases of salmonellosis simulating appendicitis have been described on numerous occasions. An excellent review of this condition and allied subjects has recently been published by Black, Kunz and Swartz.[1] Isolation of Salmonella organisms from human mesenteric lymph nodes has to our knowledge not been described. Whether the association of Salmonella organisms in both these cases is a fortuitous one or represents a true causal relationship to the symptoms described cannot be stated at the present time. A report by Rubin[2] is of some interest in this connection. The author examined mesenteric lymph glands from apparently normal hogs and cultured Salmonella organisms in 47.5% of 40 lots of animals, each lot consisting of 25 animals. A variety of Salmonella organisms was obtained from these cultures. We have consistently encouraged simultaneous histological and bacteriological examination of lymph nodes, particularly since the publication of the excellent paper on this particular subject by Weed and Dahlin.[3] Lymph node biopsies have been done in cases of mesenteric adenitis, in view of the obscure etiology of this condition. However, in several such nodes examined so far in our laboratory, we have been unable to culture micro-organisms. The bacteriological examination most likely should also be extended to include virological examination and bacteriological studies of the fecal contents of appendices. A concerted effort of this kind might establish a further etiological basis in some cases in which a mistaken clinical diagnosis of appendicitis has led to laparotomy.

With regard to treatment in such cases, antibiotic therapy seems to be indicated, at least until the true relationship between the micro-organisms isolated and the disease process has been established. Furthermore, treatment would appear to be worth while, as these patients quite likely act as carriers of potentially pathogenic micro-organisms.

SUMMARY

Two patients with suspected appendicitis were explored surgically and enlarged lymph nodes were removed in both; these revealed Salmonella organisms on bacteriological examination. The implications of these findings have briefly been discussed.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

Savory, in 1879, in his address in surgery before the British Medical Association, places himself on record as opposed to the theories enunciated by Lister. But he refers to the poisoning in our wounds as "the scourge of surgery", and remarks, "Would that I could say it was altogether a thing of the past—of history only; that we are able now to cast it out." "When," he continues, "will some successor of mine in this honourable and responsible position be able fairly to affirm so much?" Little did he suspect that the affirmation would come in a few years from the man whom at the moment he was criticising adversely, when Lister himself in turn was to deliver the address in surgery before the Association. It may be supposed that little assistance in the fight against infection could be expected from Savory when we find him stating that "No mischief of this kind lurks in fresh healthy pus." Savory, like many who accepted similar views at that time, was much influenced by the circumstance that often "one cannot successfully inoculate the healthy tissues with septic bacteria." Lister, too, be it remembered, was somewhat puzzled by that fact, and many of us remember how he welcomed the explanation which came in the demonstration of the phagocytic action of living cells by Metchnikoff in 1887, a demonstration that was the precursor of many which followed in succeeding years from a host of investigators in elucidating the complicated problem of the defensive attributes of the living tissues. Savory treated his wounds with tepid water, and recommended bread poultices. He says, "A well made bread poultice preserves ample moisture and equable warmth; it is everywhere very soft and adapts itself with singular uniformity to all irregularities of surface."—A. Primrose: Address in Surgery to the 44th Annual Meeting of the Canadian Medical Association, *Canad. M. A. J.*, 1: 611, 1911.

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SHORT COMMUNICATION

ACRIDINE ORANGE FLUORESCENCE IN CYTOLOGY OF THE CERVIX*

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THE PURPOSE of this report is to present our experience with acridine orange (AO) fluorescence in gynecologic exfoliative cytology. Consecutive cervical smears were examined and compared with parallel smears examined by independent observers using the standard Papanicolaou technique. This comparative analysis was undertaken in order to evaluate the efficiency and reliability of the AO technique.

Material

Cervical smears from 500 consecutive patients were made available to us by the British Columbia Cancer Institute. These smears were examined by the acridine orange technique. Parallel smears were examined by independent observers, using the routine Papanicolaou technique, in the department of cytology.

Methods

Cervical smears were fixed immediately in alcohol-ether (equal parts) for at least 30 minutes. They were then stained by the technique described by von Bertalanffy, Masin and Masin.[1]

Smears were:

1. Hydrated by passing them through 80%, 70% and 50% alcohol for 10 seconds each, and rinsed in distilled water.
2. Treated with 1% acetic acid for six seconds followed by rinsing in two changes of distilled water.
3. Stained in 0.1% acridine orange for three minutes.
4. Washed in M/15 phosphate buffer, pH 6.0, for one minute.
5. Differentiated in M/10 calcium chloride for 30 seconds.
6. Mounted in a drop of pH 6.0 phosphate buffer, and examined under a fluorescence microscope.

Nuclei fluoresced a bright green; cytoplasmic ribonucleic acid, a brilliant red.

Fluorescence Microscope

The Zeiss large fluorescence equipment was used, as previously described,[2] having a OSRAM H BO 200 maximum pressure mercury lamp as a source of ultraviolet light. A BG 12 exciter filter was used to give light with a wavelength of 3650 A°, this wavelength having been shown to give a maximum fluorescence. A Zeiss research microscope was used, although any conventional model is adequate. We now use a dark ground condenser for all fluorescence work since it gives better contrast, although a standard type may be used for this particular stain. OG 4 and OG 5 (yellow) barrier filters were used in the eyepiece and these resulted in a brilliant red and green fluorescence of cells on a black background.

Results

In attempting to use a basis upon which to evaluate the accuracy of the AO technique, it was necessary to utilize the high degree of accuracy obtainable with the Papanicolaou technique as a baseline for comparison. At the British Columbia Cancer Institute, where over 300 smears a day are examined, the results of yearly follow-up indicate an accuracy of 0.13% false negatives and 4% false positives (i.e. 4 proved to be negative out of every 100 reported positive smears).

Unequivocal results were obtained in 436 cases of the 500 pairs of smears examined, using the AO and Papanicolaou techniques: 410 were agreed negatives and 26 agreed positives. In the remaining 64 cases, AO technique gave 10 false positives, 9 false negatives and 45 which were regarded as suspicious but found to be negative by the Papanicolaou technique.

DISCUSSION

Conflicting results, using fluorescence microscopy and acridine orange, have been reported in evaluation and diagnosis of malignant exfoliative cytology. Several large surveys[3-6] have appraised the AO technique and found it superior to the Papanicolaou method for the detection of malignant cells. On the other hand, Umiker, Pickle and Waite[7] applied the AO technique to other areas of exfoliative cytology (sputum, stomach washings, urines, etc.) and concluded that it was less sensitive than the Papanicolaou method and not as reliable. Kornfield and Werder[8] emphasized that any young and actively growing tissue will contain sufficient cytoplasmic RNA to produce significant AO fluorescence. They point out the danger of thinking of AO as a specific cancer stain. The strongest criticism of the AO technique comes from Liu,[9] who found the cytoplasmic fluorescence non-specific and unreliable. These workers emphasize the fact that morphologic criteria need to be applied and that the morphologic detail obtained with the AO

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technique is poor compared with the Papanicolaou method.

In view of the fact that the AO technique demands an aqueous mountant having a low refractive index, compared to the Papanicolaou method using a synthetic resinous mountant with a high refractive index, it is obvious that an inferior resolution will be obtained by the former technique. In the final analysis, the diagnosis must depend upon fine morphologic detail which, theoretically, is almost impossible to achieve using a mountant having a low refractive index.

Our findings coincide with those of Umiker, Pickle and Waite,[7] Kornfield and Werder,[8] and Liu,[9] that the bright red fluorescent staining of RNA in cells is not invariably a sign of malignancy and, in general, the advantages of AO staining are outweighed by those of the established Papanicolaou technique. The value of the AO technique as a method of fast cytologic screening appears diminished by the number of false results which are obtained.

SUMMARY

In our experience, the acridine orange fluorescence technique is inferior to the routine Papanicolaou method for the detection and diagnosis of malignancy in exfoliative cytology of the cervix. Actively growing cells (basal cells, endocervical and endometrial cells) may show considerable and misleading cytoplasmic fluorescence in a smear.

Where a diagnosis could be made easily with AO staining, it could usually be made with equal ease using the Papanicolaou technique. In borderline cases a diagnosis is dependent on morphologic criteria rather than the less specific staining of RNA. Owing to the difference in refractive index of the mountants, cytologic detail is far superior in the Papanicolaou technique. Furthermore, AO smears, because of their aqueous mountant, are not permanent.

We acknowledge with gratitude the co-operation of Dr. H. K. Fidler, Dr. D. Boyes and Mr. D. Lock of the Department of Cytology, British Columbia Cancer Institute.

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MEN AND BOOKS

NOTES ON THE FOXGLOVE AND WILLIAM WITHERING

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"The use of the Foxglove is getting abroad and it is better the world should derive some instruction, however imperfect, from my experience than that the lives of men should be hazarded by its unguarded exhibition, or that a medicine of so much efficacy should be condemned and reflected as dangerous and unmanageable".

WITH THESE words, William Withering of Birmingham introduced his unique treatise on the diuretic effects of digitalis leaf. The year was 1785. Therapeutics in the modern sense was non-existent, the flourishing "science" of the day being a mystical jumble of camphor, leeches, potions and purgatives. True, digitalis leaf had been used for centuries in herbal medicines against ailments ranging from asthma to "the Kings Evill", all with varied success. The German botanist, Fuchs, first mentioned it in 1542 and named it digitalis after the common name in his country "Fingerhüt" or finger stall. Boerhaave, the great Leyden physician of the early eighteenth century, described it as poisonous, and Withering recounts with some delight M. Salernés experiments upon "a vigorous turkey cock".

> "The bird was fo much affected that he could not ftand upon his legs, he appeared drunk and his excrements became reddifh."

Dr. Withering was blessed with keen faculties and unusual interests. One must know more of the man to understand his future discovery. Young William, son of a successful apothecary in Shropshire, studied medicine at Edinburgh, receiving the degree of doctor of physik on July 31, 1776, at the age of 25. The professor of medicine at the time, William Cullen, thought highly of Withering, and his M.D. thesis on scarlatina is still regarded as a model of cautious scientific inquiry. A popular lad, he was introduced to golf by his northern friends and won his way to their hearts by learning to play the bagpipes. Upon graduation, many flattering offers of entering practice reached his desk. He selected Stafford, in South Staffordshire, where the reputation of his father and physician-uncles was high.

Patients were few at first. Idle time was turned to a new interest—botany; and between infrequent calls he dissected and made notes. Among the young man's first patients at Stafford was 17-year-old Helena Cook, daughter of a local businessman. During her long convalescence she amused herself by painting flowers, and gallant William often arrived with sprays of wild blooms, having combed the countryside for the finest and most suitable specimens. Admiration grew, botanical interests mingled with the esthetic, and the local flora scattered seeds of love. One thing led to another and by September the attractive Miss Cook became Mrs. Withering. The two were soon spending many hours in the preparation of a work later to become a classic in British botany, "The Botanical Arrangement of British Plants", and the young physician became known as the "British Linnaeus".

His interest in herbal remedies increased.

Two unconnected events in 1775 changed Withering's life. The first was his appointment as physician to the Birmingham Infirmary where he soon achieved social and professional success. The second event is best reported in his own words:

> "In the year 1775, my opinion was asked concerning a family receipt for the cure of dropsy. I was told that it had long been kept a secret by an old woman in Shropshire who had sometimes made cures after the more regular practitioners had failed and I was informed also that the effects produced were violent vomiting and purging, for the diuretic effects seem to have been overlooked. This medicine was composed of twenty or more herbs, but it was not difficult for one conversant in these subjects to perceive that the active herb could be no other than the Foxglove."

"*. . . that the active herb could be no other than the Foxglove*". Here was a simple act of genius! Two and two made four. The botanist and physician in one suspected the truth, put it to the test, and an invaluable fact was unearthed from the mystic "nothingness" of herbalism.

The late professor of therapeutics at Birmingham University, K. Douglas Wilkinson, told an interesting version of Withering's discovery, although he gave no source.

> "When [Withering] came to Birmingham he used to drive each week to see patients referred to him at the Stafford Infirmary. This was a journey of thirty miles each way and at some point the horses used to be changed. One day while the change was going on, he was asked if he would see a poor old lady with dropsy. He saw her and formed a poor opinion of her prospects. Some weeks later, when he inquired about her, he learned to his surprise that she had made a good recovery, and his astonishment impelled him to see her again, and seek the cause of her improvement which was attributed to a herb tea."

Withering first tried digitalis at Stafford and later at Birmingham, as more patients were under his care there. Of the 163 personal cases described, only one was recorded as having been treated in 1775 and five in 1776. He was struck by immediate though unpredictable success in the treatment of dropsy and after two years of random observation case notes were carefully recorded. At first there was no way of calculating the dose, and toxic effects were occasionally discouraging. He found that the administration of an infusion of 3 drams of powdered leaves boiled in 8-12 ounces of water, two spoonfuls every two hours until nausea developed, generally gave a profound diuresis, slowing the heart and strengthening the beat, with marked improvement in the patient's comfort. Such encouraging results made him less sceptical and with continued practice smaller doses effected an equal diuresis and fewer side reactions. After 10 years of empirical trial of infusions, tinctures, combinations with squill, chalk, wine or lemon, his final note is a model for the British Pharmacopoeia:

> "I still prefer the leaves . . ." (Then follows a description of their collection and dessication and "rubbing down to a beautiful green powder".)
> "I give to adults from 1-3 grains of this powder twice a day."
> "About 30 grains of the powder may generally be taken before the nausea commences."

Effects, Rules and Cautions

> "The Foxglove when given in very large and quickly repeated doses occasions sickness and vomiting, purging, giddiness, confused vision, objects appearing green or yellow, increased secretion of urine, with frequent motions to part with it and sometimes inability to retain it; slow pulse, even as slow as 35 in a minute, cold sweats, (increased salivation), convulsions, syncope, death . . .
> "When given in a less violent manner it produces most of these effects in a lower degree . . .
> "At first I thought it necessary to bring on and continue the sickness in order to ensure the diuretic effects. But it soon appeared that the diuretic effects would often take place first . . . and the directions were therefore enlarged thus—'Continue the medicine until the urine flows or sickness or purging takes place.' I found myself safe under this regulation for two or three years, but at length cases occurred in which the pulse would be retarded to an alarming degree, without any preceding effect. The direction therefore required an additional attention to the state of the pulse.
> "Let the medicines, therefore be given in the doses and at the intervals mentioned above; let it be continued until it acts either on the kidneys, the stomach, the pulse or the bowels; let it be stopped upon the first appearance of any one of these effects."

The present Pharmacopoeia adds to these effects certain abnormalities of cardiac rhythm which occur with digitalis intoxication or associated potassium deficiency. Withering never used a maintenance dose of the drug and, although he knew that the pulse was strengthened, suggested that digitalis acted primarily upon the kidneys, and not the heart. He commented on the irregularity of the

pulse in only one case, that of Miss Hill of Ashton by N....., a woman between 40 and 50 years of age.

> "I found her nearly in a state of suffocation; *her pulse extremely weak and irregular,* her breath very short and laborious, her countenance sunk, her arms of leaden colour, clammy and cold. She could not lie down in bed and had neither strength nor appetite, but was extremely thirsty. Her stomach, legs and thighs were greatly swollen, her urine very small in quantity, not much more than a spoonful at a time and that very seldom."

Miss Hill made a remarkable recovery with the course of digitalis and was still alive nine years later when Withering wrote the above account. She required digitalis every few months when edema developed.

> "I have been more particular in the narrative of this case, partly because Dr. Darwin has related it rather imperfectly in the notes to his son's posthumous publication, trusting I imagine to memory . . ."

Charles Darwin, son of Erasmus, referred to above, and uncle of the naturalist, Charles, had been a medical student at Edinburgh but died there of meningitis in 1779. His father published Charles' M.D. thesis in 1780 and appended reports of nine cases of dropsy treated with digitalis, one of them being that of Miss Hill. These cases are therefore the first account in any language of the use of digitalis as a diuretic. It seems clear, however, that the therapy was Withering's original idea, for his report of the case, which he saw in consultation with Darwin in 1776 reads: "Dr. Darwin very politely acceded to my proposition [the use of digitalis] *and as he had never seen it given* left the preparation and dose to my direction."

Dr. Jonathan Stokes, a friend and physician at Stourbridge, wrote in February 1779 to the Medical Society of Edinburgh about Withering's discovery and by late 1779 the drug was in general use in the Infirmary there. In 1783 it was included in the Edinburgh Pharmacopoeia, "but", says Withering, "from which it will be again very soon rejected, if it should continue to be exhibited in the unrestrained manner in which it has heretofore been used at Edinburgh, and in the enormous doses in which it is now directed in London." He was right; but further caution brought it into general use later. Withering recommended the use of digitalis in cases of dropsy, anasarca, ascites and hydrothorax. He found it of little value in pulmonary tuberculosis, ovarian cysts, hydrocephalus, alcoholic cirrhosis with ascites and asthma. Once Withering saw a travelling Yorkshire tradesman who had been treated by his wife for asthma. She stewed a large handful of foxglove leaves and gave him the concoction to drink. He was extremely ill and had a pulse rate of 40 but recovered. "This good woman knew the medicine of her country but not the dose of it."

Dr. Withering lived long enough to see his discovery widely used with considerable success and for the last years of his life enjoyed the praise and respect of both the medical and botanical worlds of his day. He continued to be in great demand as a medical consultant but poor health prevented much activity. During the autumn of 1793 he was particularly distressed. On October 5, a friend called, saw him fading and is reported to have sadly commented, "The flower of English physicians is indeed withering." Within a few hours, he died.

"An account of the Foxglove" rewards its reader with its clarity and precision. Humanity and intelligence peek through those brown dog-eared pages and there is amusement as well as the finest in medical education within. Fine copies of the first edition are to be found in a few Canadian libraries, among them the University of Toronto Medical Library and the Osler Memorial Library, McGill University, Montreal; and although the books are no longer chained to reading stalls, the librarians there will wish otherwise, knowing there's many a physician and botanist who would give a handsome price for that musty bit of paper, dried ink and ragged hide.

This essay owes its origin to the interest shown by some Aberdeen medical students in the therapeutic history of digitalis, and to my pleasure in finding a plant, unknown in my country, but used daily by its physicians, blooming so commonly in Aberdeenshire, Scotland.

My thanks are due the staff of The Burroughs-Wellcome Historical Library, London, England, who allowed me the use of the following books (unchained).

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

A principle in treatment enunciated by Magendie is worthy of record, when he remarked, "Our only usefulness in the presence of nature, which in general tends to normal conditions, consists in not interrupting her; it is only now and then that we can aspire to be sufficiently skilful to aid her." The same idea was suggested by Benjamin Franklin, when he wrote regarding doctors, "He's the best physician that knows the worthlessness of the most medicine."

The man imbued with the true scientific spirit will often cull treasures of great therapeutic value from most unpromising sources, and we have no right to discard any scientific truth as irrelevant to practical medicine. It is quite remarkable to note how many discoveries have been made by observing the simple processes of nature.—A. Primrose: Address in Surgery to the 44th Annual Meeting of the Canadian Medical Association, *Canad. M. A. J.*, 1: 615, 1961.

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MERCI À MONTRÉAL

IN 1535 Jacques Cartier discovered an Indian village named Hochelaga on an island in the St. Lawrence River. Here, in the French settlement of Ville-Marie, Paul de Chomedey, Sieur de Maisonneuve, founded the town of Montreal on May 18, 1642. In 1832 this flourishing metropolis was incorporated as a city. From June 19 to 23 this year, Canada's first city passed another milestone when it played host to some 2100 intrepid voyageurs who converged on this history-drenched island, bearing their staffs of Aesculapius, to attend the 94th Annual Meeting of the Canadian Medical Association. Although the luxury and convenience of the Queen Elizabeth Hotel is a far cry from the primitive lodge in which the aboriginal hosts of old Hochelaga greeted their first guests from France over four centuries ago, many of the tradition-minded conventioneers of 1961 still strove to keep alive the unrestrained exuberance of the Indian pow-wow of an earlier day.

In terms of the numbers of registrations the 94th was the largest annual meeting in the history of the Association. Details of the program are reported elsewhere in the Journal. Some of its highlights that impressed this observer were:

—The successful innovation of "teaching sessions" in the scientific program.

—The full day of sessions devoted entirely to matters of medical economics.

—The impressive galaxy of personalities from the upper echelons of academic medicine who came from across Canada to attend the meeting throughout its entire duration.

—The neatness and despatch with which General Council disposed of its formidable agenda within the allotted two and a half day period without restriction of debate on the reports of some 25 committees.

—The long-awaited announcement of the personnel and terms of reference of the Royal Commission on Health Care; the presence of the Commission Chairman and his participation in the program adding to its timeliness and significance.

—The formal dignity of the Annual General Meeting where Senior Membership in the Association was conferred upon nine of its distinguished elder statesmen and where Dr. Wilder Penfield presented the C.M.A. with a gavel fashioned from a branch of Hippocrates' plane tree from the island of Cos.

—The remarkable teaching session in the Montreal Museum of Fine Arts which took the form of an audience-participation type of program entitled "Dégustation de vins de France".

By historical coincidence, in the same month fifty years ago, the city of Montreal played host to the 44th Annual Meeting of the Canadian Medical Association, an event which likewise provided editorial inspiration to Sir Andrew Macphail, our more illustrious predecessor of that era. His reflections on that occasion afford an interesting and enlightening commentary on the similarities and differences between our Association's annual meeting of today and that of half a century ago.

"The forty-fourth meeting of the Canadian Medical Association which was held in Montreal on June 7th, 8th and 9th, 1911, was one of the largest in the history of medicine in Canada. About four hundred and twenty-five members attended, and at various times more than a hundred members were present at the various sections.

"There was no dearth of entertainment, but it was kept in due subordination to the main purpose of the meeting. No one could regret that the traditional 'banquet' was not revived. A mass meeting is scarcely the occasion when a man may eat with comfort, drink with advantage or talk with pleasure and profit. The business was transacted promptly and little time was spent in futile discussion. Indeed the ground had been prepared so carefully that little was left for the members except to assent to what had been done.

"The scientific work was of a very high order in respect of the papers which were presented and of the discussion which they aroused, and they were presented by men who were well qualified to speak for the profession. There were singularly few absentees, and that class of members has been eliminated who are content to have their names upon the programme without much thought to the obligation which thereby devolves upon them. Sir James Barr fulfilled his undertaking to be present and his address was listened to with much interest; but two other eminent men, namely, W. J. Mayo and Howard A. Kelly, were unable to attend. Naturally there was disappointment in the minds of many members, which would suggest to the executive in future the wisdom of putting forward no attractions which do not possess a reasonable certainty of being exercised."

The foregoing sentence bears plaintive witness to the fact that throughout the years since doctors first began to organize professional meetings, the

best laid schemes of program committees "gang aft a-gley". Should those concerned with local arrangements for the 94th Annual Meeting harbour recriminations about any of their plans that failed to materialize as anticipated, they may find some consolation in the frustrations experienced by their counterparts charged with the planning and conduct of the Association's 1911 meeting. In this respect we are informed that—

"By an oversight, the paper of Professor E. J. Evatt, of Winnipeg, who was present, was not read. This is a matter of regret as the subject 'A Few Notes on The Prostatic Urethra' is an extremely interesting one."

Or again, that—

"Unfortunately, the syphilitic lesions in the rabbit, which were to be demonstrated by Dr. R. P. Campbell of Montreal, had not matured sufficiently to be demonstrated to the Section [of Laboratory Workers], although in the course of the last year he has had a succession of animals which have shown most typical lesions, affording abundant spirochaetes."

If any such mishaps did occur to mar this year's meeting, they were certainly not apparent. As they did on the last occasion on which the C.M.A. met in Montreal ten years ago, our hosts of the Quebec Division extended themselves to their hospitable utmost, and the newly elected President of the Association, his gracious wife, all of the local committees, and the Division as a whole merit sincere gratitude and commendation for the excellence of their arrangements and the efficient manner in which these were carried out.

The Cause of Primary Diabetes Mellitus

CONSIDERING the accumulated knowledge regarding the metabolic disturbances of diabetes, the paradoxical conclusion may be justified that we are practically as far removed from complete understanding of this branch of pathological physiology as our predecessors were 50 years ago. In those days there was only one problem in diabetic research, the origin of the sugar excreted in the urine. Non-utilization and overproduction of glucose were the only two theories of etiology and both had their proponents who used them to explain all of the metabolic phenomena of diabetes. Since then the centre of gravity in diabetic research has shifted from time to time in various directions. Insulin, glucagon, the adrenal and pituitary glands have all been shown to exert important actions on carbohydrate metabolism and more recently certain enzymes are being investigated regarding their role in this disorder.

There is no doubt that diabetes mellitus due to primary disease of the pancreas is very rare indeed. It is now well established that a pancreatectomized human requires on an average 35 to 40 units of long-acting insulin daily for the control of his diabetes. Some cases have been recorded in which even lesser amounts were required and occasional patients have died of hypoglycemia in spite of complete removal of all pancreatic tissue.[1]

The underlying cause of primary diabetes mellitus is still unknown. The concept that dominated diabetic research after the discovery of insulin, that diabetes was basically an inherited deficiency of insulin production by the pancreas, has been revived by Loubatières in France. According to this investigator, hypoglycemic sulfonureas have a beta-cell trophic action that results in an increase in the number of beta cells and in the volume of islets of Langerhans, frequently at the expense of centro-acinar cells and excretory canaliculi.[2] It is also recalled that spontaneous remission of diabetes in humans has been known to occur and is now being reported more frequently. The exciting possibility suggested by Loubatières that chemotherapy could produce regeneration of the pancreatic islets must, of course, await further confirmation, but support for these claims has come from certain other centres.

A different concept, discussed in a recent article in the *Lancet*,[3] is based on the theory of the existence of insulin antagonists in human plasma. Antagonism to insulin has been recognized for years and the literature contains many reports of cases in which enormous doses of insulin had to be given to patients over shorter or longer periods of time; doses in the order of 1500 units or more daily are not unknown. The mechanism of this antagonism apparently resides in the globulin fraction of the serum, is thought to be allergic in nature, and can at times be overcome by corticosteroid administration.

A different form of insulin antagonism has been identified more recently by Vallance-Owen and Lilley[4] and by Lowy, Blanshard and Phear[5] who have reported the results of their latest experiments with this insulin antagonist which is attached to the albumin fraction of the serum. Lowy *et al.* support Vallance-Owen's findings that this antagonist inhibits the response of muscle to insulin but fails to antagonize the action of insulin on the glucose uptake of fatty tissue. Although similar antagonism is present in the serum albumin of normal subjects, it is less active than that found in the serum of diabetics who require insulin therapy. Vallance-Owen postulated in 1958 that "whatever the site and mode of action of insulin in carbohydrate metabolism, it has first to overcome the antagonistic activity of the plasma albumin fraction".[6] He now considers it possible that this form of increased antagonism to insulin constitutes the primary abnormality in essential diabetes mellitus and that it is an inherited trait of persons who develop this disease.

These findings, if confirmed, would represent the development of the diabetic process somewhat as follows. Antagonism by the albumin of the plasma

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causes a relative insufficiency of insulin which in turn stimulates increased production of insulin by the pancreas; when the latter becomes exhausted, true insulin insufficiency follows. It is well known that untreated juvenile diabetics have at times been found to possess circulating insulin in their blood in considerable amounts. Pre-diabetics may even have increased blood levels of insulin. When these pre-diabetics or uncontrolled diabetics are placed on a proper regimen, it appears that their blood insulin activity is increased or that the antagonism to insulin is reduced.

These studies have resulted in attempts to improve the methods for serum insulin assay through the use of fatty tissue for the uptake of glucose, as fatty tissue is not influenced by the insulin antagonist. The failure of the albumin insulin antagonist to inhibit glucose uptake by fatty tissues *in vitro*, when insulin or insulin-containing serum is added, suggests to Vallance-Owen that "obese diabetics are obese because of their diabetes", since the insulin antagonist does not prevent glucose uptake by fatty tissue. These observations raise the hypothetical possibility that other obese persons, especially those who have extreme difficulty in reducing their weight, have some disturbance of the balance between insulin and its albumin antagonist.

Attractive as this hypothesis of the cause of diabetes may be, even cursory reflection on the known facts about diabetes indicates that it will not satisfactorily solve all of the questions raised by this disorder. The influences of growth hormone and of corticosteroids on the activity of the antagonist have not been proved unequivocally. Although this theory could account for the progressive decrease in insulin requirements by some patients in the end stages of diabetic nephropathy because of their low serum albumin levels and hence smaller amounts of circulating antagonist, spontaneous remissions or the rare spontaneous cures of diabetes are not so readily explained. When insulin requirements vary without apparent reason, is it because the activity of the serum antagonist fluctuates? Do tolbutamide and other oral hypoglycemic agents act by suppressing the activity of the insulin antagonist? Finally, if this hypothesis should be confirmed as explaining the basic cause of primary diabetes mellitus, will it enable physicians to devise more effective treatment of this disorder? W.G.

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WHY DOCTORS LEAVE EAST GERMANY

ALTHOUGH no official or reliable statistical data are available relevant to the numbers of physicians who have taken abrupt and unofficial leave from East Germany for refuge in the West, a recent report from Switzerland (*Schweiz. Aerztezig.*, 41: 819, 1960) suggests that the extent of this medical migration is not inconsiderable. We are informed, for instance, that from the staff of the City Hospital of East Berlin alone, six doctors fled to the West German Republic in one year, and that during the same year seven members of the medical staff of another East German hospital made their escape to the West.

In an attempted analysis of the motivation that prompted the flight of these physicians from the communistic areas of influence it is noted that, by and large, the majority of medical men on the staffs of East German hospitals do not actively engage in politics or hold membership in any political party, devoting their energies instead to their professional responsibilities. There are exceptions, however, and some hospital chiefs are very eager Communists indeed. The director of the surgical clinic of the University of Leipzig, we are told, demands that his staff physicians "assume political responsibility", participating in political conferences every two weeks, organizing discussions on political issues and listening to words of wisdom from authorities in the Communist hierarchy. Our source of information tells us that not a few of these doctors took their departure because they felt incapable of maintaining the pretense of accepting political opinions that they could never hold.

Unwillingness to have their children brought up in the Communist faith provided an important added impetus for their departure to the West.

To the date of our latest information at least, doctors from the communist zone have been permitted to participate in scientific meetings in West Germany and are enjoined on such occasions to propagate the cause of communism to their West German audiences.

Drug supplies from the West are still available in satisfactory quantities in hospitals of the Soviet zone. Although instruments, on the whole, are of decidedly inferior standards, x-ray apparatus and highly technical equipment such as heart-lung machines which are imported from the West are of high quality. There is a general shortage of nursing personnel throughout East Germany.

Political pressure is exerted upon the medical profession by both direct and indirect means. Thus, "political reliability" as well as professional qualifications determines the appointment of doctors to academic posts in the Communist zone.

This information probably constitutes no surprising revelation, but it is of interest to encounter a commentary on this subject in a medical periodical.

Letters to the Journal

MEDICAL SECTION, CANADIAN PHARMACEUTICAL MANUFACTURERS ASSOCIATION

To the Editor:

Your reference in the March 25 issue (*Canad. M. A. J.*, 84: 668, 1961) to the Medical Section of the C.P.M.A. was very timely, and it gives me the opportunity to inform the medical profession of one of our present projects.

Many of the problems existing between the drug industry and the medical profession in Canada are of concern to the physicians within the drug industry. Formed in the years since the war to fill the needs brought about by growth and development within the industry, the Medical Section of the Canadian Pharmaceutical Manufacturers Association comes to serve, as an affiliated society of the Canadian Medical Association, as the natural liaison between the profession and the industry. Within this capacity the members of the Medical Section are required to speak for the medical profession on those problems relating to it, and to advise management accordingly.

Confronting these issues, it has become clear to the members of the Section that one of the fundamental weaknesses in the association between the profession and the pharmaceutical industry lies in the area of communication. This is nowhere more evident than at present in the area of medical opinion on the points of contact between industry and physicians.

Precisely what does the medical profession think about the drug industry, and who speaks for the medical profession? With what accuracy do some self-appointed spokesmen reflect the views of the profession at large? Each and every doctor holds views of varying intensity on any and every contact with the pharmaceutical industry, and these views are often of a conflicting nature, a fact which appears all too often ignored by some who purport to speak for the medical profession at large.

Faced with this problem, the Medical Section of the C.P.M.A. endeavours at this time to ensure, in so far as it is able, to reflect as clearly as possible the representative views of the profession. Towards this end the members of the Section will attempt to meet with groups of doctors across the land, and to discuss with them, at both formal and informal meetings, the issues which appear to be in conflict. This will essentially constitute an exercise not of interpreting the drug industry to the physician, but of gathering from him the comments and suggestions on what he feels to be desirable and undesirable in the relationship between himself and the pharmaceutical industry.

Meetings under the aegis of the Canadian Medical Association are being held with physicians from all the major centres in Canada. The information so gathered will be supplemented by a questionnaire to be sent to approximately 3000 physicians in all parts of the country, and from this total information it is hoped to establish a reliable index of medical opinion for the guidance of the Medical Section members in their advice to industrial management.

Anything less than a representative opinion is considered to be grossly inadequate in view of the complexity of the issues involved. While it is only natural to anticipate some areas of disagreement between a profession and an industry, more particularly under the stress of rapid change and development, it is nonetheless an historical fact of some note that the association between doctors and the drug industry has been based on an attitude of mutual interdependence and respect. That it should remain so is to the interest of everyone involved.

J. R. MACDOUGAL, Chairman,
Public Relations Committee,
Medical Section—C.P.M.A.

CARE OF THE DYING

To the Editor:

In a recent issue of the Statistical Bulletin of the Metropolitan Life Insurance Company the figures for the number of Americans dying in hospital is reported to exceed those dying out of hospital. As a reflection of the increasing use being made of these institutions in the treatment of serious illness, the deaths occurring in hospital have risen from 45% in 1949 to 53% in 1958. Figures are not available for Canada, but the trend appears to be in the same direction.

Whatever else might be said about admitting to hospital those who might prefer to die at home, and whose dying is only prolonged in hospital, the increasing number of those who end their days in a hospital ward brings with it an increasing responsibility on the part of the medical profession to assume its share in providing for the spiritual needs of the sick and dying. If the modern hospital has overcome the traditional dread of its being little more than a morgue, the change is all for the good, but if in the process it has lost sight of the crucial needs of the dying, it has merely exchanged the fear of dying for the fear that dying has no meaning. To many patients death is the culmination of living, and in the modern hospital with its emphasis on diagnosis and treatment there is little place for dying, and even less for the preparation which precedes it. To even the critically sick the attitude is one of hopeful expectancy, and while this might serve to explain the indifference on the part of the medical profession for the solace which many patients appear to need and expect in the face of death, it does not excuse it. Too often the attending doctor is himself to blame for the lack.

This is not to suggest that a doctor should act towards his patient in the role of the minister or priest, although it might be said that if the medical profession is to give anything more than lip service to the concept of treating the whole person, it must commit itself in the spirit of the clergy, if not in their methods or approach. It does suggest that inherent in the responsibility of attending the sick is the recognition that more than strictly medical care is required, and that the doctor must be more than merely acquiescent in providing it.

Under "Points of View" in *Lancet* (1: 761, 1961), Dr. Hugh Kolly comments: "The doctor's co-operation

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[with the clergy] should not depend on his own religion but only on that of his patient: even if he has no religious feelings he must give the chaplain whatever help the patient needs and demands . . . in other words, the doctor must accept that the chaplain has a function."

This is perhaps obvious, but it seems often assumed by the attending doctor that anything relating to other than strictly medical care is either irrelevant in the total care of the patient, or at best the responsibility of someone else, minister or priest, who will somehow inform himself on the state of the patient in hospital, and render whatever services may be necessary. Too often the clergy feel out of place in a busy hospital, and if it is still the courtesy of some of the older doctors to make a point of including the minister in the treatment and care of the critically sick, the tradition seems confined to them. To the majority of other doctors, and particularly to the more recent graduates, the role of the minister commences when all hope of medical recovery has failed. Even then, the suggestion to relatives that a minister be called carries with it admission of defeat few doctors willingly make, preferring instead to do nothing in face of the inevitable except to increase the sedation so as to make the end as painless as it is meaningless.

If the greatness of medicine lies in the admission of its own limitations, the trend towards more deaths taking place while under the care of a doctor in hospital allows the medical profession ample opportunity of attesting to it.

R. W. SHEPHERD, M.D.
Medical Director,
Ciba Company Ltd.,
Dorval, Que.

GENERAL PRACTICE EXCHANGE: OFFER FROM SCOTLAND

To the Editor:

I am a medical practitioner engaged in a general group practice in Scotland.

I would like to gain some experience with Canadian general practice and hope to plan an exchange, for six months or so, with an interested Canadian doctor; alternatively I would consider doing a six months' locum tenens.

The Canadian Medical Association has told me that reciprocal registration privileges exist between the General Medical Council of Great Britain and the licensing authorities of the following provinces: Alberta, Saskatchewan, Manitoba, Nova Scotia, Prince Edward Island and Newfoundland. Accordingly, an exchange would require to be with a doctor from one of these provinces.

This practice, situated six miles from Edinburgh, is in a coal-mining area. Although I would like especially a practice in the mining areas of Nova Scotia or southern Alberta, I would be interested equally in other areas.

If any of your readers are interested in considering such an exchange, I would be very pleased to send them details of this practice, the local country, remuneration, etc.

H. M. S. NOBLE, M.B., Ch.B.
The Hill, Broomieknowe,
Lasswade, Midlothian,
Scotland.

THE LONDON LETTER

NAMING THE DELINQUENT

The disciplinary agency for minor delinquencies in the National Health Service in Britain is the local health executive council, and so far it has been their practice not to name doctors or dentists appearing before them, even if a fine or other punishment is inflicted. If of course the charge is more serious, then the delinquent is hailed before the General Medical Council (say, in the rare case of false certification or financial irregularity) or may even come into the hands of civil justice. For some reason not entirely clear, the Labour Party has from time to time pressed the Minister of Health to publish the names of these delinquents, and in May an indignant member said in Parliament, "Even if this is about the only official secret that the Government are able to keep, is it not a public scandal that doctors, who are paid out of public funds and who let the public down, should be covered by this conspiracy of silence?" This display of moral indignation is of course the stock in trade of all oppositions, and it is doubtful whether the member was on firm ground in saying that the public was strongly in favour of naming the guilty. However, the Minister stood firm and said quite rightly that these people were guilty of breaches of contract and not of breaches of the law. Indeed, if all the people of England who let the public down by doing a poor job are to have their names published, extra editions might perhaps be necessary from time to time.

Mr. Powell, the Minister, amplified his statement later when addressing the Winchester Division of the B.M.A., by saying that the doctor's or dentist's name "ought no more to be blazoned in public than that of the decorator who agrees to knock £10 off his contract price for house painting because he admits to having made a mess of the ceilings".

The British Medical Association and the British Dental Association have both gone on record as agreeing with this standpoint. The dentists are particularly anxious, because so often these minor cases concern a poorly fitting set of dentures, and it seems rather excessive to make a newspaper story out of this.

TV IN THE MEDICAL SCHOOL

The days when the lecture was the main means of medical instruction are over, and the progressive medical educator is well aware of the need to keep an eye on the new media such as radio, films and TV, in case there should prove to be some advantage to himself through their use. But medical educators are conservative and they tend to look askance at new things, especially when the new things are better known for their so-called entertainment value than for their serious employment.

It was therefore not surprising to find that when the Association for the Study of Medical Education staged a two-day symposium on TV in the medical school recently at the London Hospital, with American and German participation, there was a certain amount of scepticism in the air. However, those who had used television for teaching pre-clinical and clinical subjects put forth a good case for its investigation, and did not

make the mistake of making an emotional appeal do duty for a commonsense one. It was quite surprising to find colleagues from the United States urging their British friends not to spend too much money on their excursions into TV, to discard any ideas of studio performances or colour TV, and to make the medium do what nothing else could do, and concentrate on that. It seems that the uses of TV can be summarized as enabling people to see what they could not see before (as in endoscopy), to see better than they had done before (as in the operating room), and to see in greater numbers. Particular fields singled out for attention were radiology, where TV monitoring can replace screening with advantage, endoscopy, demonstrations of anatomy before large classes (beautifully shown to the audience in a demonstration of the muscles of the hand), demonstrations of physiology (where it has the advantage over film that the tempo can be adapted to the class), histology (where it is likely to replace all other methods), and psychiatry. A large class can follow a psychiatric interview over a few TV monitor screens, and sense the drama of the case in a unique way. One participant said that this was the only way to teach psychotherapy.

Canadian educators will no doubt be well represented at the next symposium on this subject, to be held under the sponsorship of the American Medical Association in Chicago early in October.

Reducing the Drug Bill

The Minister of Health is still on the warpath, seeking ways of reducing the nation's drug bill, and his most recent attempt has been to invoke a power not usually exercised by government outside the field of national defence, by which he can break the power of a patentee of any drug to set the level of his royalty from the patent. At present, government can acquire drugs for the hospital service only from the patentee or licensee (in the case of a foreign patent), though some hospitals have already bought drugs from abroad at prices less than those charged in Britain by purchasing from unlicensed sources.

As an experiment, the Minister is going to advertise for tenders for the supply of three classes of drug: tetracyclines, chloramphenicol and the chlorothiazide group. Both British manufacturers and importers will be able to tender, and bargains will be made direct with patentees about payment of royalties, so that the Crown can get the most favourable price.

This could work out to the advantage of some firms who at present are suffering from purchase of pirated versions of their drug bought from abroad, but in general the first reaction of the industry in Britain was to express anxiety that there might not be sufficient royalties coming in to provide for research and development.

The Times remarks, "Cheaper drugs would naturally be welcome and it has to be proved that they cannot safely be obtained. It would be wrong, however, to exaggerate the significance of the drug bill as an item in the cost of the health service and positively dangerous if, in spite of official assurances, the quality of the products did decline. If, furthermore, research has to be curtailed, the saving would in a national perspective be an expensive one, and it is questionable whether bidding against foreign firms who may be prepared to sell surpluses abroad at lower prices than at home amounts to fair competition." Naturally there has been speculation about the singling out of one industry for this type of treatment, and it may be asked whether the government intends to break patents in buying other goods.

Medical School Adopts a Population

The Times reports that the medical school of Birmingham University is likely to have a new type of facility in the future, if plans mature for the medical "adoption" of 100,000 people in three suburbs of the city by a health centre. Birmingham has for some time been an active centre of "social medicine" (not "socialized medicine"), and some of the teaching staff feel that the modern medical student is not getting sufficient contact with the population in its social environment, and is therefore not learning about such urgent topics as mental health and the care of the ageing. The new centre would provide comprehensive medical services for the population of the suburbs involved and would include the present Queen Elizabeth Hospital, a maternity hospital, and units for the care of the aged and the mentally ill. It would act in association with the general practitioners of the suburbs and the public health services. It would also give the students an idea of the whole of medicine, and perhaps bring a more personal or human touch into the hospital service.

Treating the Psychopath

Lord Nuffield has done it again, and handed over a large donation to King Edward's Hospital Fund for London, this time the sum of £100,000 to build two centres for research and treatment of psychopaths. One will be for long-term residential treatment of potentially dangerous psychopaths who are "not motivated to seek treatment", and people with severe antisocial tendencies such as alcoholism and drug addiction, persistent cheque forgery, "neurotic delinquency", promiscuity and homosexuality. These will be the first facilities available in Britain for this specific purpose, and one centre will deal with outpatients and the other with inpatients. "A high standard of living facilities will be planned, as patients naturally do not like squalid surroundings." Research will be a feature, and it will certainly be needed, because the outsider may be forgiven for thinking that the medical profession (or anyone else, for that matter) has as yet no clue to the handling of these disturbers of the peace. The sociologist, Lady Wootton, who never hesitates to break a lance with the medical profession, was quick to point out that the plain English of the phrase "not motivated to seek treatment" implies that psychopaths will be compelled to go into these centres, and also that it is not criminal to be promiscuous, and that promiscuity raises moral issues and not medical ones. She says (with some justification) that "to enforce compulsory medical treatment on the promiscuous is to allow the medical profession to set themselves up as arbiters of our morals." The learned lady certainly has a point, and if the wording were interpreted widely, that £100,000 might not go very far in this age of shaky sexual morals.

S. S. B. GILDER

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MEDICAL NEWS IN BRIEF

CAUSES OF POSTOPERATIVE WATER AND ELECTROLYTE RETENTION

In a study of water and electrolyte metabolism in 58 women during and after gynecological operations, daily control of urine volume, specific gravity and sodium and potassium excretion was started two days prior to operation and carried out until the eighth to tenth postoperative day.

Although previous reports describe an increased excretion of antidiuretic substances in the urine in the postoperative period, Friedberg *et al.* (*Schweiz. med. Wchnschr.*, 91: 441 and 470, 1961) could find antidiuretic activity in the plasma only during the operative procedure or, at the most, two and a half hours after the operation. No antidiuretic activity was demonstrable in any of their patients thereafter.

Aldosterone secretion was found to be increased to a significant extent only in four patients on the first day after operation. In the remaining patients there was no such postoperative increase. This was an unexpected finding because of the well-known occurrence of postoperative retention of sodium and chloride and marked potassium excretion. Postoperative oliguria of short duration was not statistically significant; only in the first twelve postoperative hours was any reduction of volume and increase of salt content of the urine demonstrable. Sodium excretion was reduced significantly in the first few days, particularly between the second and the fourth days, whereas potassium excretion was increased considerably on the first day and was markedly decreased between the fourth and sixth days.

Glomerular filtration, investigated by creatinine clearance in 16 patients, was decreased on the second and fourth postoperative day, as compared to preoperative findings. In these patients plasma volume (Evans-blue) showed a significant decrease on the second postoperative day and this was paralleled by diminished sodium excretion. It was assumed on the basis of these findings that postoperative retention of salt is not humoral in origin but results from change in plasma volume.

POSTPARTUM CARDIOMYOPATHY

In 13 patients reported on by Reid (*South African M. J.*, 35: 165, 1961) in whom heart failure developed post partum, all had typical "South African cardiomyopathy", a condition in which the heart is largely free of fibrosis.

Nutritional factors were studied by means of a dietary history, from the clinical appearance of the patient, from the results of vitamin replacement, by determining plasma protein levels and by liver biopsy, but no evidence of any specific nutritional deficiency was obtained.

The cases presented did not differ from a comparable series of men with cardiac myopathy, except in age and prognosis. The mean age of the 13 postpartum patients was 29 years; that of the males was 41 years. This may indicate that the causative factors of cardiomyopathy may be exaggerated in the puerperium, resulting in earlier onset of the disease. No cases were found in nulliparous African women. In this series two patients had twin deliveries, and these were the only individuals completely refractory to therapy. The other postpartum patients improved more after therapy than the male patients, but in none was the condition reversed completely.

It is thought that some unknown postpartum process precipitates heart failure in patients with cardiomyopathy, itself of unknown etiology; that the cardiomyopathy may be fundamental and the postpartum process transitory.

The relation between postpartum South African cardiomyopathy and the puerperal cardiomyopathies described in people of European origin is difficult to assess. On the basis of the criteria used for inclusion in the present series, no individually reported European case could be included. The condition was not seen among Asian patients treated at the same hospital as the African subjects in this series, although their numbers are the same as Africans in the general population served by the hospital. Disease states have been reported in American Negroes that would meet the criteria for inclusion in the present series.

A NEW HAZARD OF UNDERWATER SWIMMING

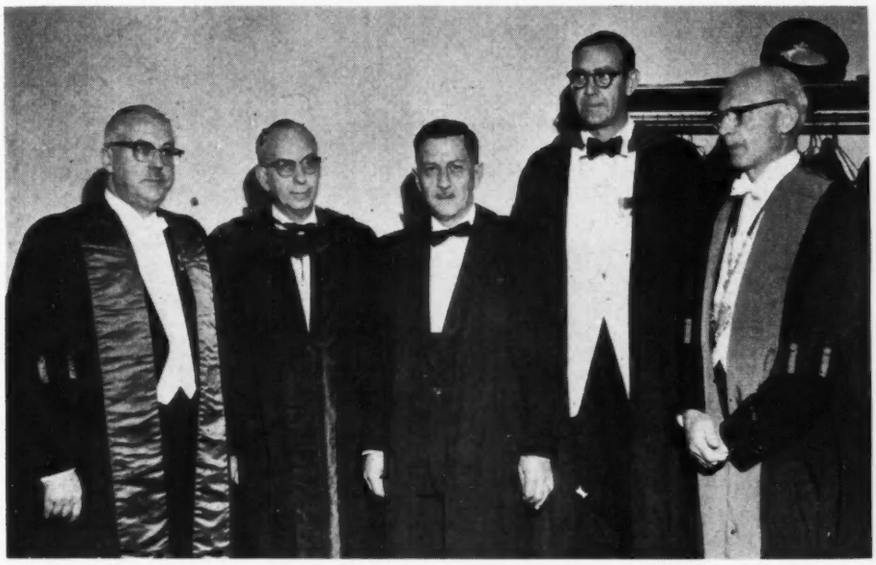
An annotation in a recent issue of the *British Medical Journal* (1: 1956, 1961) calls attention to the serious danger in hyperventilating before swimming underwater. Professional swimming coaches have long known that sudden loss of consciousness is not at all uncommon while training for "plunge" competitions where participants hyperventilate, for a minute or two before diving, to increase performance. "Plungers" and some underwater swimmers can lose consciousness soon after immersion. Hyperventilation, by lowering pCO_2, causes constriction of the cerebral vessels and dilatation of muscle vessels. The syncopal attack is induced by the performance of a Valsalva maneuver immediately after hyperventilating, and the loss of consciousness is startlingly sudden. This maneuver is done by straining against a blocked airway as in the common practices of straining during defecation, coughing and in many forms of muscular exertion. Because much blood is trapped in the peripheral veins, cardiac filling pressure and stroke output may fall to low levels. The tense, streamlined attitude of the "plunger" and the exertions of the underwater swimmer after hyperventilation provide suitable conditions for this "plunger's syncope". Craig (*J. A. M. A.*, 176: 255, 1961) describes eight patients who lost consciousness but survived after swimming underwater and five others who drowned under similar circumstances. He stresses the dangers of previous hyperventilation; it is the young, supremely fit individual who is most likely to respond in this way. Athletic instructors, swimming teachers, lifeguards and all those interested in water safety should be warned that there are grave risks attached to this common practice.

(Continued on advertising page 32)

THE NINETY-FOURTH ANNUAL MEETING OF THE C.M.A.

UST ten years after it last met in Canada's leading metropolis the Canadian Medical Association returned to Montreal to hold its ninety-fourth annual meeting from June 19 through June 23, in the elegant setting of the Queen Elizabeth Hotel. The total registration was the largest in the history of the Association, including as it did, some 1630 members and other registrants, and 485 ladies.

Other guest speakers on the scientific program included Dr. C. Miller Fisher, Assistant Professor of Neurology at Harvard Medical School; Dr. Maurice Mayer, Associate Professor in the Faculty of Medicine of the University of Paris; and Dr. Leroy D. Vandam, Clinical Professor of Anesthesia at Harvard Medical School.



Three fraternal delegates to the Annual General Meeting of the C.M.A. who brought greetings from their respective organizations are seen with the President and the President-Elect of the C.M.A. Left to right: Dr. Gerald W. Halpenny, President-Elect; Dr. Milford O. Rouse, Dallas, Texas, official delegate of the American Medical Association; Dr. Emile Blain, Montreal, official delegate of l'Association des Médecins de Langue Française du Canada; Dr. D. B. Stewart, Kingston, Jamaica, official delegate of the Jamaica Branch of the British Medical Association; and Dr. R. MacGregor Parsons, President of the C.M.A.

An eminently successful innovation in the scientific program was the introduction of teaching sessions designed to provide the practising physician with current information concerning developments in treatment and diagnosis of a broad range of disorders encountered in many fields of medicine.

Another feature that was incorporated into the scientific program for the first time was the simultaneous French-English translation service provided at sessions held in the Grand Ballroom and Marquette, Jolliet and Duluth Rooms of the hotel. Such recognition of the Association's two official languages was particularly apropos at this meeting in the heart of French Canada.

The twelfth Lister Lecture was delivered in general session on June 22 by Dr. Hugo Rosenqvist, Surgeon-in-Chief of the Södersjukhuset, Stockholm, Sweden. This lectureship was established by the C.M.A. in 1924 when the first Lister Lecture was delivered by Dr. John Stewart of Halifax, a distinguished pupil of the famous surgeon in whose honour the lectureship is named.

All photographs by Business & Industrial Photographers Ltd., Queen Elizabeth Hotel, Montreal.

Some of the numerous highlights of the week-long activities are described in the editorial pages elsewhere in this issue, and as observed therein, our hosts of the Quebec Division in general and those responsible for the planning and conduct of all aspects of the local program are deserving of high praise and a resounding expression of gratitude for the warmth of their hospitality and the excellence of their arrangements on which the eminent success of the ninety-fourth annual meeting was based.

ANNUAL GENERAL MEETING

After the entry of the platform party at 8.30 p.m. on Wednesday, June 21, the 94th Annual General Meeting in the Grand Ballroom of the Queen Elizabeth Hotel opened with the singing of "O Canada".

The invocation was delivered by the Rev. R. Douglas Smith, Officiating Minister of Dominion Douglas United Church, Westmount, after which the members and their guests were welcomed by the Association's President, Dr. R. MacGregor Parsons. In addition to the officers of the C.M.A., fraternal delegates, senior members-elect and other dignitaries, the platform party was graced by the presence of the Honourable Alphonse Couturier, Minister of Health of the Province of Quebec.

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Distinguished platform guests at the Annual General Meeting include Dr. Adolphe-Charles Bohémier, Dr. Wilder Penfield, Dr. Emile Blain, Dr. J.-B. Jobin, the Rev. R. Douglas Smith, Dr. Alphonse Couturier, Dr. A. D. Kelly, Dr. R. MacGregor Parsons, Dr. G. E. Wodehouse, Dr. E. C. McCoy and Dr. Gerald W. Halpenny.

The President, Dr. R. MacGregor Parsons and Mrs. Parsons, with President-Elect Dr. Gerald W. Halpenny and Mrs. Halpenny, prior to the Annual General Meeting.

Recipients of Senior Membership in the C.M.A. are seen with Dr. A. D. Kelly, General Secretary. From left to right: Dr. George Herbert Clement, Vancouver; Dr. Morley Counsellor Bridgman, Oliver, B.C.; Dr. Donald Faison McIntyre, Winnipeg; Dr. William J. Deadman, Toronto; Dr. Donald Grant Dingwall, Dryden, Ont.; Dr. Kelly; Dr. Charles-Adolphe Bohémier, Montreal; Dr. Wilder Graves Penfield, Montreal; Dr. David Sclater Lewis, Montreal; and Dr. Daniel Finlayson MacInnis, Shubenacadie, N.S.

Fraternal delegates Dr. Milford O. Rouse of Dallas, Texas, representing the American Medical Association; Dr. Emile Blain of Montreal, representing l'Association des Médecins de Langue Française du Canada; and Dr. D. B. Stewart of Kingston, Jamaica, official delegate of the Jamaica Branch of the British Medical Association, were introduced by the President, and it was announced with regret that Dr. W. H. C. Masters, official delegate of the Bermuda Branch of the British Medical Association, was unable to attend.

Isaac Edwin Crack of Hamilton; John Thomas Phair, King, Ont.; Samuel James Streight, Port Credit, Ont.; Archibald Stanley Kirkland, Rothesay, N.B.; and Chester Harris of Marystown, Nfld., who were not present at the Annual General Meeting.

Dr. Gerald W. Halpenny of Montreal was then installed as President of the Canadian Medical Association by his predecessor in office, Dr. R. MacGregor Parsons.

Members of the Platform Party at the Annual General Meeting, a colourful event of the 94th Annual Meeting, are: Dr. Murray S. Douglas, Windsor, Ont., Chairman of the General Council; Dr. Gerald W. Halpenny, Montreal, President-Elect of the C.M.A.; Dr. R. MacGregor Parsons, Red Deer, Alta., President of the C.M.A.; and the Reverend R. Douglas Smith, B.A., B.D., D.D., of Montreal.

Owing to his commitments in the Canadian Arctic, His Excellency Major-General Georges P. Vanier, Governor-General of Canada, was prevented from being present to receive honorary membership in the Association, which was conferred upon him *in absentia*. It is noteworthy that this marked but the third time in C.M.A. history that this honour has been bestowed upon a non-medical recipient, the other two honorary memberships having been presented to Governor-General Vanier's predecessor, The Right Honourable Vincent Massey, and to His Royal Highness The Prince Philip, Duke of Edinburgh.

Senior Membership in the C.M.A. was then conferred upon nine distinguished elder statesmen of Canadian medicine in the persons of Drs. Morley Counsellor Bridgman of Oliver, B.C.; George Herbert Clement of Vancouver; Donald Faison McIntyre of Winnipeg; William James Deadman of Toronto; Donald G. Dingwall of Dryden, Ont.; Charles-Adolphe Bohémier, David Sclater Lewis and Wilder Graves Penfield, of Montreal; and Daniel Finlayson MacInnis of Shubenacadie, N.S.

Additional Senior Memberships have been or will be conferred by their Provincial Divisions upon Drs. Melvin Graham of Ponoka, Alta.; Donald Neil MacCharles of Medicine Hat; Walker Stewart Lindsay of Saskatoon; Frederick Arnold Clarkson of Toronto;

THE PRESIDENT'S INAUGURAL ADDRESS

I deeply appreciate the confidence that has been placed in me by my election to the office of President of the Canadian Medical Association, and I shall do my best to prove worthy of this great honour. I am aware of the grave responsibility of this position and will spare no personal effort to maintain the traditions and further the beliefs of our great Association.

Throughout the near-century of its existence, the Canadian Medical Association has faced many problems, but none so critical as the one which now challenges our profession and for which there is no precedent to guide us, in the long annals of medical history. We must find new paths to replace a way no longer adequate. If through apathy or lack of unity we let others force decisions upon us, generations of inferior medical care could result.

We must work together with the strength of unity, we must take time from the individual demands upon us, to scan the whole horizon of medicine. We should without delay bring our collective views and opinions to the Royal Commission on Health Services, to give this body all the available help and knowledge at our disposal. This is a pressing challenge, for the days in which to accomplish the task may be truly numbered.

I should like to express my sincere thanks to all members of the Program Committee and to the members of the Quebec Division who have worked long hours planning the many details of this convention. We are very grateful to the members of the secretariat from Toronto for their co-operation and their help.

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Dr. Gerald W. Halpenny presents the Past-President's Badge of Office to Dr. R. MacGregor Parsons.

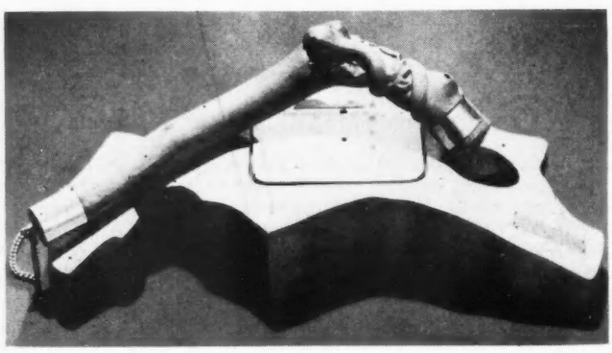
> A mes confrères de la langue française: veuillez accepter mes sincères remerciements pour votre assistance et votre appuie, dans la préparation du programme pour cette réunion annuelle.

May I also say a word of thanks to those of my colleagues who have carried on my work while I was busy preparing for this Annual Meeting.

In conclusion, on behalf of my wife and myself, may I say a very special word of thanks to the many members of the Ladies' Committee, who have given generously of their time and assistance in planning the Ladies' Program.

We sincerely hope that you will enjoy this meeting in Montreal.

Following his inaugural address Dr. Halpenny presented the Past-President's badge to Dr. R. M. Parsons.



The gavel presented to the C.M.A. by Dr. Wilder Penfield. It is fashioned from a branch of Hippocrates' plane tree from the Island of Cos.

The meeting closed on an impressive note when Dr. Wilder Penfield presented the Association with a gavel fashioned from a branch of the Mediterranean plane tree beneath which, it is said, Hippocrates taught medicine to his students on the Greek Island of Cos, in the fifth century B.C. The branch was removed earlier this year by permission of the Governor of Cos, and was carved by Mrs. Kenelm Winslow. The holder for the gavel was made of Canadian maple, cut in the shape of the island of Cos by Mr. and Mrs. Winslow. On the holder is a metal sounding plate upon which are engraved quotations from the Oath of Hippocrates: *"I will keep pure and holy both my life and my art"*; and from his Book of Aphorisms: *"Life is short, the art so long."*

After the National Anthem was sung, the members and guests adjourned to Dr. and Mrs. Halpenny's reception in the Convention Foyer, and later to dancing in the Grand Ballroom.

MEETINGS OF GENERAL COUNCIL

The proceedings of the meetings of General Council which were held in the Grand Ballroom of the Queen Elizabeth Hotel on Monday, June 19, Tuesday, June 20 and Wednesday morning, June 21, will be published *in extenso* in the September 2 issue of the Journal, in the Transactions of the 94th Annual Meeting.

Particularly impressive was the unhurried manner in which Council disposed of its extensive agenda within the allotted two and a half day period during which the detailed and comprehensive reports of some 25 committees, officers and staff members of the Association were presented and subjected to critical scrutiny and unrestricted debate.

An element of drama was introduced on Tuesday, June 20, when the General Secretary, after being called from the meeting to receive a telephone message from the nation's capital, returned with the following announcement:

AN ORDER IN COUNCIL ESTABLISHING A ROYAL COMMISSION ON HEALTH CARE

The Committee of the Privy Council have had before them a report from the Right Honourable John G. Diefenbaker submitting that, while recognizing that the power to make laws relating to health services is, except in limited fields, within the jurisdiction of Provincial Legislatures, it is considered to be in the public interest to have a comprehensive and independent study made of the needs of the Canadian people for health services and the resources available to meet such needs with a view to recommending methods of ensuring that the best possible health care is available to all Canadians.

The Committee, therefore, on the recommendation of the Prime Minister, advise that:

Chief Justice E. M. Hall, Saskatchewan (Chairman)
Mr. M. Wallace McCutcheon, Toronto, Ont.
Prof. O. J. Firestone, Ottawa, Ont.
Dr. C. L. Strachan, London, Ont.
Dr. Arthur F. VanWart, Fredericton, N.B.
Dr. David M. Baltzan, Saskatoon, Sask.
Miss Alice Girard, Montreal

be appointed Commissioners under Part I of the Inquiries Act to inquire into and report upon the existing facilities and the future need for health services for the people of Canada and the resources to provide such services, and to recommend such measures, consistent with the constitutional division of legislative powers in Canada, as the Commissioners believe will ensure that the best possible health care is available to all Canadians and, in particular, without restricting the generality of the foregoing, the said Commissioners shall inquire into and report upon:

(a) The existing facilities and methods for providing personal health services including prevention, diagnosis, treatment and rehabilitation.
(b) Methods of improving such existing health services.
(c) The correlation of any new or improved program with existing services with a view to providing improved health services.
(d) The present and future requirements of personnel to provide health services.
(e) Methods of providing adequate personnel with the best possible training and qualifications for such services.
(f) The present physical facilities and the future requirements for the provision of adequate health services.
(g) The estimated cost of health services now being rendered to Canadians, with projected costs of any changes that may be recommended for the extension of existing programs or for any new programs suggested.

(h) The methods of financing health care services as presently sponsored by management, labour, professional associations, insurance companies or in any other manner.

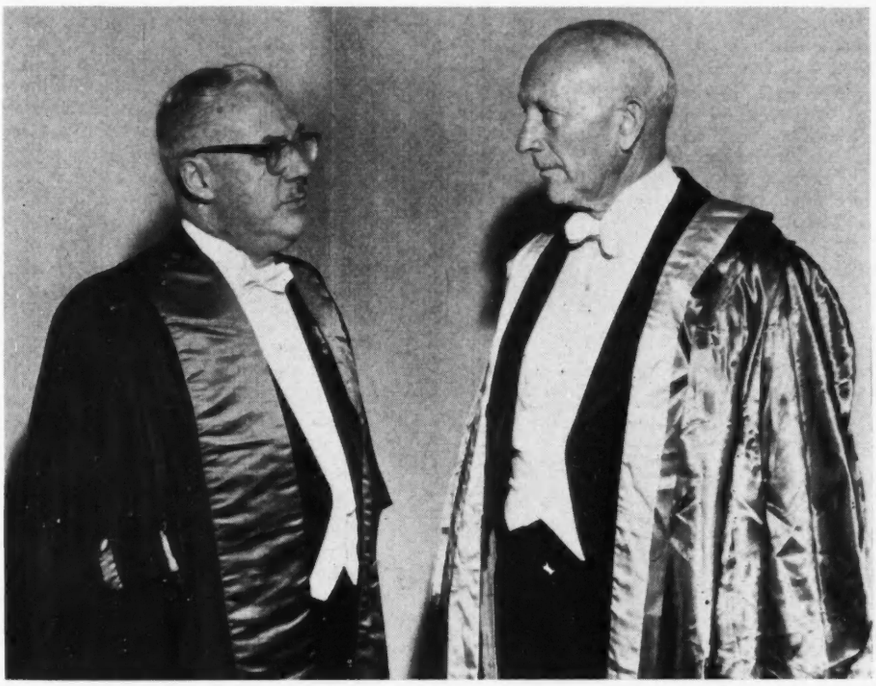
(i) The methods of financing any new or extended programs which may be recommended.

(j) The relationship of existing and any recommended health care programs with medical research and the means of encouraging a high rate of scientific development in the field of medicine in Canada.

(k) The feasibility and desirability of priorities in the development of health care services.

LUNCHEON FOR MEMBERS OF GENERAL COUNCIL

On Monday, June 19, members of General Council and their wives gathered for an official luncheon in the Duluth Room of the Queen Elizabeth Hotel after which Dr. R. MacGregor Parsons delivered the President's Valedictory Address, the text of which was published in its entirety in the July 8 issue of the Journal.



Dr. Gerald W. Halpenny, President-Elect of the C.M.A., is seen with Dr. Wilder Graves Penfield, just before the Annual General Meeting at which Dr. Penfield was awarded Senior Membership in the C.M.A.

(l) Such other matters as the Commissioners deem appropriate for the improvement of health services to all Canadians.

The following officers of the Association were elected for 1961-1962:

President-Elect—Dr. M. R. MacCharles, Winnipeg, Manitoba.

Chairman of General Council—Dr. T. J. Quintin, Sherbrooke, Quebec.

Honorary Treasurer—Dr. G. E. Wodehouse, Toronto, Ontario.

Divisional Representatives on the General Council:

British Columbia—Dr. F. S. Hobbs

Alberta—Dr. E. F. Donald

Saskatchewan—Dr. H. D. Dalgleish

Manitoba—Dr. R. Richardson

Ontario—Drs. R. H. McCreary, P. Bruce-Lockhart and W. W. Wigle

Quebec—Drs. R. Du Berger and T. Primrose

New Brunswick—Dr. P. Melanson

Nova Scotia—Dr. R. O. Jones

Prince Edward Island—Dr. J. A. McMillan

Newfoundland—Dr. J. B. Roberts

RECEPTION AND DINNER TO GENERAL COUNCIL

The Quebec Division's reception and dinner to General Council on Tuesday evening, June 20, were featured by the address of the Honourable Jean Lesage, Premier of Quebec, and a gay program of amusing entertainment arranged by Dr. George Strean and his Committee. The complete text of Premier Lesage's address follows.

Lorsque vous avez bien voulu m'inviter à participer aux importantes assises médicales que vous tenez en ce moment à Montréal, j'ai hésité quelque peu en raison de la très lourde tâche que m'imposaient alors les trauvaux sessionnels. Cette session qui a duré sept mois est terminée depuis dix jours —et, je vous l'assure, une des raisons pour lesquelles j'en étais heureux, c'est que celà me permettait d'être des vôtres ce soir.

Your President had some very kind words to say about me just now. I wish to thank him from the bottom of my heart. It is very consoling for a man in politics to realize that the efforts he has devoted to his Province and his country are sometimes appreciated in a sphere such as yours.

Dr. Halpenny is considered, and quite rightly so, to be a past master in his profession. He has spared neither his time, nor his devotion, nor his intelligence to make your Association one of the most influential groups in the country. Today his altruism has received its just award in his election

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as national president of the Association, after having served as treasurer for a long time. Your choice of Dr. Halpenny brings honour not only to the Canadian Medical Association, but to the Province of Quebec as well.

It gives me a great deal of pleasure to welcome you who come from the other provinces as friends. Distant friends, perhaps, because you only visit us once every five years, but friends that we are very happy to meet.

The Canadian Medical Association was born in the City of Quebec on October 9, 1867, the year that the young Canadian nation, finally aware of its future and its extraordinary potential, became united under Confederation. Your elders thought it advisable to give your professional society a structure similar to that established by our constitution for our political life. I congratulate you on this. Like Canada, you have grown in age and in wisdom and today you have become adults. The one hundred and sixty-seven pioneers who met in Quebec 94 years ago put down the roots. In 1961, their heirs number more than 14,000, of whom there are 2300 in the Province of Quebec. Thus you constitute a social and economic force that is essential to the common good. You have successfully carried out your mission, which is to promote health, wipe out sickness, improve medical services and maintain the honour and integrity of the medical profession.

Seen conversing prior to the Dinner to General Council are (left to right): Dr. A. D. Kelly, General Secretary of the C.M.A.; Dr. R. MacGregor Parsons, President; The Hon. Jean Lesage, Premier of Quebec; and Dr. Gerald W. Halpenny, President-Elect.

You will soon be a hundred years old, and like the country itself, you are preparing to celebrate this memorable anniversary in a suitable manner. I know that at that time you will come back to the Ancient Capital, the cradle of the nation. We will welcome you with open arms. I am deeply convinced that in 1967, if God spares me, I shall be here to bid you welcome . . . as head of the Quebec Government.

We all owe a tremendous debt of gratitude to the physician. For over three centuries, he has been associated with the life of our people, and throughout that time, he has played an important part in the social progress of this province.

A few moments ago, Dr. Halpenny spoke about the Hospital Insurance Act which has been benefiting the population of the Province of Quebec since January 1, 1961. This piece of legislation is particularly close to my heart, because with the improvement that we have brought to our educational system and to our cultural life, it has been the cornerstone of my party's policy.

Last April, in speaking to the members of the Quebec Hospital Association, meeting in this same hotel, I said: "Your collaboration is indispensable to us. If it were to be refused to us or even restrained, our program for today, as well as tomorrow's progress, would be paralysed."

To those doctors of my province who are listening to me tonight, I make the same appeal in emphasizing a most important point that I wish to make clear: *this highly outstanding social law is based on the professional conscience of the physician.* Without his intelligent co-operation, it becomes useless. In fact, he alone is the judge. He has the sole responsibility of admitting a patient to hospital, and is the only one to decide when he is to leave.

As in the other provinces, our Hospital Insurance Act is intimately linked with the practice of the medical profession. In fact, it is impossible to provide hospital treatment for a whole population without providing for the development of those who will have the task of giving this treatment.

What is the government's role as regards medicine?

A satisfactory answer still remains obscure. Governments strive to provide legislation which will serve the best interests of its people. Medicine is doing its utmost to provide the best medical care for the people. It is obvious, therefore, that we have the same objectives and ideals. Surely then, having these things in common, we can work together to marshal that knowledge which is the heritage of our civilization and extend its usefulness beyond the limits of its present boundaries.

I hope that the government will not seek in vain for help from the medical profession for concrete guidance in solving the problem of providing the best possible medical care for every citizen, while at the same time safeguarding and maintaining the high standards of the profession for future generations.

As Dr. J. A. McMillan, of Prince Edward Island, wrote recently (page 441 of Volume 84 of the *Canadian Medical Association Journal*, dated February 26, 1961): "We must rid our conversation of all such emotionally charged expresions as 'state medicine, socialized medicine, winning the battle, fighting bureaucrats and politicians; and express ourselves ably and well in the matters which we should be so specially trained to discuss."

Here lies the immediate challenge to your profession.

Your approach to the future must be *united, realistic, honest* and *unselfish.*

Yours should be the guiding hands in the inevitable changes; upon you lies the responsibility of overcoming the medical shortcomings and needs created by today's complex world. I think you must accept the fact that the solution to a nation's health problems are too complex and gigantic to be solved without the aid and co-operation of governments.

Your guidance is all the more necessary because the unlimited and measureless miracle of science could create unnecessary misery in the future, should they fall into untrained and unskilled hands. The sternest challenge that faces you is to continue to attract into your profession the same dedicated type of individual who has been its most valuable heritage throughout its long history. If your morale is lowered, if you are going to face a changing world with reluctance, resentment or criticism, you could undermine and damage one of the greatest achievements of our civilization.

Personally, I have a deep and ever-present conviction that the greatest opponents of socialism are those who, being all for evolution, follow a flexible policy adapted to circumstances.

I will even add an afterthought which will be pessimistic and optimistic at the same time—pessimistic for those who support an egotistical policy of serving private interests; optimistic for those who are sufficiently broad-minded and whose hearts are big enough not only to believe in, but also to practise, the moral principle that there are no rights without responsibilities. This afterthought reminds us of both our responsibilities and the advance of sound social and economic doctrine (I could say strategy). Only evolution can prevent revolution.

Making medical and hospital care available to all is an essential part of a well-conceived social security program.

This social security which causes the raising of eyebrows among reactionaries, this security which, when it is put into operation, is pompously referred to as "socialization" by those professional exploiters of prejudice—do you know what His Holiness Pope Pius XII said about it on December 24, 1952? He called it "a formula for Christian solidarity which will cause the disappearance of the gross inequalities between individuals and peoples."

which are dictated to their more or less compliant will. I honestly believe that this thesis will prove particularly useful to you in the carrying out of your mission and in the application of the principles which I have just laid down.

* * *

Mesdames et Messieurs de l'Association Médicale Canadienne, et plus particulièrement ceux d'entre vous qui exercez votre sacerdoce (je plains le médecin que ce mot ferait sourire) qui exercez, dis-je, votre sacerdoce dans la province de Québec . . . je suis profondément imbu de ce qui me paraît un corollaire inévitable de la conception démocratique du gouvernement.

Depuis que l'humanité existe, elle semble prendre un malin plaisir, un plaisir . . . (je m'excuse d'employer un mot que vous comprenez professionnellement mieux que moi) un plaisir masochiste à se déprécier elle-même. Il est vrai, hélas! que les défaillances de la nature humaine fournissent de nombreux arguments aux cyniques, aux pessi-

Dr. Gerald W. Halpenny, President-Elect of the C.M.A., talks with Dr. Alphonse Couturier, Minister of Health for the Province of Quebec; Dr. Wilder Graves Penfield, Montreal; and Dr. René-L. DuBerger of Sherbrooke, Que., newly elected President of the Quebec Division of the C.M.A.

Like everyone else, and more particularly as a lawyer and heir to a Latin tradition that puts the accent on reasoning and dialectics, I like a discussion in which, taking nothing for granted, we try to prove everything that is put forward. However, if revelation exists in faith, it seems to me that it should also exist in charity.

It is impossible for me, and I say it with pride, it is impossible for me not to get mad at an egotist or at those who are politically backward, and to whom it must be proved that lack of money should not be an obstacle to the recovery of one's health. *I cannot admit, for anything in the world, that someone will live because he can pay for treatment, and that someone else will die because he cannot pay for the same treatment.*

One would have to have no sense of values, one would have to have remained deaf to six thousand years of biblical tradition and two thousand years of Christianity, not to be able to recognize without being shown that, no matter what the material sacrifice, we must preserve that infinitely precious asset which is human capital.

I am sure that we agree completely on this point, and now, with your kind permission, I shall leave on this note of harmony, after just a few more words in my mother tongue on a subject which is very close to my heart.

In a well-organized society and in a real working democracy, the best laws (and I mean of course those laws which are abided by) are those that are both inspired and agreed upon by the interested parties, instead of those

mistes, voir aux idéalistes désabusés. Et cependant . . . sans aller jusqu'à l'aveuglement de Rousseau qui croit que "l'homme naît bon et que la société le déprave", je crois que l'humanité est meilleure que l'opinion qu'elle entretient d'elle-même. Je crois qu'il existe, malgré des différences énormes de conception, un sens de l'honneur et une honnêteté fondamentale dans tout individu dont la responsabilité n'est pas nettement diminuée.

Je crois surtout que lorsque l'on demande à l'individu de se juger lui-même, de *décréter sa propre loi*, on est presque toujours agréablement surpris de l'objectivité et surtout de l'élégance morale dont il est capable de faire preuve. En effet, je crois que dans cet amas de contradictions qu'est l'homme, il y a également un idéaliste qui sommeille . . . un idéaliste que la crainte du ridicule, la crainte d'être dupe, porte à se terrer ou à porter un masque. Il y a dans tout homme normal une noblesse qui remonte à la surface quand, au lieu de la nier cyniquement, on fait un acte de foi en lui demandant de se manifester.

Ce qui est vrai pour l'individu est encore plus vrai pour les Associations. *On ne se grandit pas de ce que l'on arrache à la communauté mais de ce que l'on lui apporte!* Appelez-moi "Don Quichotte" si vous voulez, mais vous verrez qu'une telle conception de l'association sous toutes formes et dans toutes ses modalités sera celle qui triomphera dans une société future dont j'ignore si l'avènement est imminent ou lointain, mais dont je veux modestement préparer les voies dans la mesure de mes moyens et de mes forces.

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Imbus du principe de servir, les médecins de la Province vont collaborer, j'en suis convaincu, sans arrière-pensée avec le Gouvernement pour mettre de l'ordre dans un domaine névralgique qui, vous l'avouerez avec moi, en réclame tragiquement!

En recommandant à la Législature un projet de loi des hôpitaux, vous ne vous laisserez, j'en ai l'assurance, guider que par un seul principe: celui de supprimer impitoyablement tous les abus, quels qu'ils soient, quels que soient ceux qui les commettent, tous les abus, dis-je, qui puisse contrecarrer et faire calomnier votre magnifique mission.

Au début de ce discours, j'ai dit en anglais, en parlant de l'assurance-hospitalisation, que cette loi sociale d'une importance extrême s'appuie en fin de compte sur la conscience professionnelle du médecin. C'est à cette même conscience, *mais à une conscience devenue unanyme,* que je demande de *transcender* les intérêts de groupe pour s'élever, comme vous le désirez tous au fond, jusqu'à la mission sociale.

Vous saurez, j'en ai pleinement confiance, recommander à la Législature un projet de loi que ne sera pas un grillage très fin et très fort autour d'une "chasse gardée", mais une garantie que l'idéal qui, au meilleur jour de votre vie, vous a fait choisir votre profession, pourra se manifester dans l'exercise de celle-ci. L'égoïsme d'un groupement n'est pas plus noble que l'égoïsme d'un individu ou que l'égoïsme à deux.

En somme, je vous demande de servir de modèle et d'encouragement aux autres associations . . . je vous demande de prouver que ce qui fait la grandeur de l'homme, c'est d'être exigeant d'abord envers lui-même, surtout quand il s'agit de servir l'humanité . . . je vous demande enfin, pour résumer ma pensée en une formule aussi concise que possible:

Prenez votre idéal et faites-en une loi!

Three distinguished physicians who participated in the Scientific Program: Dr. Hugo Rosenqvist of Stockholm, Sweden; Dr. Harry S. Morton of Montreal, Chairman of the Scientific Program Committee; and Dr. Maurice Mayer of Paris, France.

RELIGIOUS SERVICES

On Friday evening, June 16, members of the Executive Committee and their guests were invited to attend the ceremony of Bar Mitzvah in Montreal's Temple Emmanu-el. This impressive service commemorating the transition of a Jewish youth to manhood was conducted by Rabbi Stern, whose sermon dwelt on the traditional record of Jews in their honour of the art of healing and their recognition of its dual mission with religion, as indicated by the laws of health recorded in the Book of Leviticus, Chapters 12 to 15. He noted that at least 4000 years ago the Jews had a ministry of health that was perpetuated by later priests and rabbis.

This double ministry directed toward the spirit and the body was personified in the *Code for Physicians* composed by Moses Maimonides, rabbi and physician (1135-1204 A.D.):

O God, Thou has formed the body of man with infinite goodness; Thou hast united in him innumerable forces incessantly at work like so many instruments, so as to preserve in its entirety this beautiful house containing his immortal soul and these forces act with all the order, concord, and harmony imaginable. But if weakness or violent passion disturb this harmony, these forces set against one another and the body returns to the dust whence it came. Thou sendest then to man Thy messengers, the diseases which announce the approach of danger, and bid him prepare to overcome them. The Eternal Providence has appointed me to watch o'er the life and health of Thy creatures. May the love of my art actuate me at all times, may neither avarice, nor miserliness nor the thirst for glory or a great reputation engage my mind; for, enemies of truth and philanthropy, they could easily deceive me and make me forgetful of my lofty aim of doing good to Thy children. Endow me with strength of heart and mind, so that both may be ready to serve the rich and the poor, the good and the wicked, friend and enemy, and that I may never see in the patient anything else but a fellow creature in pain.

If physicians more learned than I wish to counsel me, inspire me with confidence in and obedience toward the recognition of them, for the study of the science is great. It is not given to one alone to see all that others see. May I be moderate in everything except in the knowledge of this science; so far as it is concerned, may I be insatiable; grant me the strength and opportunity always to correct what I have acquired, always to extend its domain; for knowledge is boundless and the spirit of man can also extend infinitely, daily to enrich itself with new acquirements. Today he can dicover his errors of yesterday, and tomorrow he may obtain new light on what he thinks himself sure of today.

O God, Thou has appointed me to watch o'er life and death of Thy creatures; here am I ready for my vocation.

Dr. R. MacGregor Parsons, President of the C.M.A., and Dr. G. W. Halpenny, President-Elect, participated in the service, on the completion of which the guests adjourned to a lavish buffet banquet in the basement of the Temple.

The Jewish Sabbath service was held at Congregation Shaar Hashomayim, Westmount, at 9 a.m. on Saturday, June 17.

Medical Sunday was celebrated on June 18 with a Protestant service in Dominion Douglas United Church, Westmount, and Roman Catholic masses in Mary Queen of the World Cathedral at 10 a.m. and 11 a.m.

The Reverend R. Douglas Smith, Officiating Minister of Dominion Douglas United Church, conducted the Protestant service. The title of his sermon was "Alive or Living". The reading of the Psalm was led by Dr. Eleanor Percival, representing the Federation of Medical Women of Canada. Dr. R. M. Parsons, President of the C.M.A., and Dr. Murray S. Douglas, Chairman of General Council, read the lessons from *John* 5: 1-14 and *Romans* 8: 31-39, respectively. Dr. Walter Lloyd-Smith, an elder of Dominion Douglas Church, led the congregation in a prayer of thanksgiving and intercession, and Dr. G. W. Halpenny, President-Elect of the C.M.A. and a member of the congregation, extended a message of welcome to members of the Association on behalf of the church. An interesting feature of the musical portion of the service was the vocal contribution by a talented quartet composed of Drs. Robert Sweet, Lester McCallum, Kenneth Nickerson and Eric Larking. Following the service, coffee was served in the church hall by the Federation of Medical Women of Canada.

The Hon. Jean Lesage, Premier of Quebec, and Mme. Lesage (at his right) chat informally with the wives of C.M.A. officials, Mrs. Normand Belliveau, Mrs. J. M. Denault, Mrs. Gerald W. Halpenny and Mrs. R. MacGregor Parsons.

SOCIAL EVENTS AND ENTERTAINMENT

Featured at the Montreal Museum of Fine Arts throughout the period of the 94th Annual Meeting was an exhibition of sculpture and paintings entitled "Doctors and Art". This display, sponsored by the Quebec Division of the Association in conjunction with the Museum, consisted of some 170 works of art from personal collections of doctors in the Montreal area. A committee of C.M.A. members worked with Museum officials in preparing lists and visiting doctors' homes over a period of two and a half months before the final selection was made. The exhibit included examples of Canadian paintings from Krieghoff to the present day, as well as originals by such famous European artists as Renoir, Utrillo, Dufy, Modigliani and Henry Moore.

On Sunday, June 18, a "get acquainted" coffee party was held for all members and their guests, in the Mackenzie Room of the Queen Elizabeth Hotel.

A unique event on the social program, the first of its kind in the history of C.M.A. meetings, to the best of our knowledge, was the remarkable soirée at the Montreal Museum of Fine Arts on Monday evening, June 19, which was billed as a "Dégustation de vins de France". (For the information of peasants, this was a Wine-Tasting Party.) Dr. Thomas Primrose and his local committee from the Quebec Division who laboured long and assiduously in planning this occasion may find some reward for their efforts in the general conviction that this was a most delightful experience for those who were fortunate enough to obtain their tickets before the supply was exhausted. En route along the Primrose path through the Museum's galleries, dedicated bacchants first prepared a foundation of hors d'œuvres (referred to by our host as "the blotting-paper course"), and then proceeded through an increasingly pleasant haze created by a carefully chosen selection of twelve imported French wines, ranging from Pouilly-Fuisse and Riesling to the champagnes. Incidental gastronomic diversions along the way included such gourmet's delights as a generous selection of Canadian, English and French cheeses, with a groaning board loaded with high-cal pastries providing the *coup d'état*. Throughout this latter-day festival of Bacchus, guests were admonished to observe the following DINNER RULES, as printed in the attractive and decorous souvenir menu:

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Mrs. R. MacGregor Parsons receives the Past-President's Lady's Pin from Dr. Gerald W. Halpenny, President of the C.M.A. Dr. Murray Douglas of Windsor, Ont., Chairman of the General Council, looks on. This was the first such presentation in the history of the C.M.A.

"Guests in an ebrious state will not be accommodated. The wines, most scrupulously selected to accompany and to spice the taste of each dish, must be imbibed with the dishes to which they have been designated. Conforming with this ruling, glasses will be removed with each service even if they have not been emptied. It is absolutely forbidden to smoke before the dessert, and the guest who does so scarcely merits the title of 'gourmet'. Since this occasion tends exclusively to enhance the Art of Good Eating, it is forbidden, under penalty of expulsion—to talk 'business'—furthermore, at these dinners the following subjects must be avoided: politics, religious beliefs or personal opinions of the members or their guests regardless of profession or social position."

On Thursday evening, June 22, the delegates and their guests were entertained at a colourful civic reception and buffet in the picturesque Chalet atop Mount Royal, as guests of the City of Montreal.

LUNCHEONS

The following luncheons were held by various organizations throughout the week of the 94th Annual C.M.A. Meeting:

Monday, June 19—The Canadian Tuberculosis Association; Council of the Canadian Rheumatism Association.

Tuesday, June 20—The Canadian Thoracic Society.

Wednesday, June 21—The Quebec Division of the Canadian Medical Association (Luncheon and Annual Business Meeting).

Thursday, June 22—The Association of Surgeons of the Province of Quebec.

Friday, June 23—The Canadian Medical Protective Association.

LADIES' PROGRAM

Under the chairmanship of Mrs. G. W. Halpenny, her co-chairman Mrs. N. J. Belliveau, Deputy-Chairman Mrs. Antonio Cantero and Treasurer Mrs. T. Primrose of Montreal, an active women's committee composed of wives of doctors of the Quebec Division worked industriously since last fall preparing a diversified program for the entertainment of their 485 visitors from all parts of Canada, the United States and abroad. An interesting highlight of the week's activities was the luncheon address on Thursday, June 22, by Mrs. William Mackersie, President of the Woman's Auxiliary of the American Medical Association. Mrs. Mackersie, a Canadian by birth, from Belwood, Ontario, discussed the importance of the Auxiliary in supporting the objectives and program of the medical association and the need for such an organization to promote unity and co-operation among the increasing number of medical groups. An additional ladies' luncheon was held on Wednesday, June 21, in the Montreal Museum of Fine Arts.

Sightseeing tours, a fashion show and the ladies' golf tournament on Thursday, June 22, were other attractions of a wide-ranging program of ladies' activities. A brochure containing information on shopping, dining and local places of interest was provided for registrants by the Ladies' Shopping Committee.

Morning coffee, served daily between 9.30 and 11.30 a.m. in the St. Laurent Room of the Queen Elizabeth Hotel, provided opportunities for meeting old friends and making new acquaintances.

In addition, the ladies participated in all of the social events and entertainment on the general program and were invited to attend the Annual General Meeting and the sessions on Medical Economics.

The following ladies served as chairmen of the various local committees on arrangements: Mrs. Roger Lapointe, Mrs. H. S. Morton, Mrs. S. A. MacDonald, Mrs. Paul Robert, Mrs. L. Gérin-Lajoie, Mrs. George Strean, Mrs. J.-L. Léger, Mrs. G. Earle Wight, Mrs. Jacques Bruneau, Mrs. Gordon Young, Mrs. Jacques Genest, Mrs. E. A. Stewart Reid, Mrs. C. Miller Ballem, Mrs. Gaétan Jary, Mrs. Jean Piette, Mrs. Paul Weil, Mrs. James H. Darragh and Mrs. Maurice Doray. Honorary members of the Ladies' Committee included Mrs. Frank S. Patch, Mrs. D. Sclater Lewis, Mrs. Renaud Lemieux, Mrs. Léon Gérin-Lajoie, Mrs. Sylvio LeBlond and Mrs. René Du Berger.

Mrs. William Mackersie, President of the Woman's Auxiliary of the American Medical Association, with the Chairman of the Ladies' Committee, Mrs. Gerald W. Halpenny, wife of the President of the C.M.A.

MEETINGS OF SPECIALIST SOCIETIES AND RELATED ORGANIZATIONS

The following specialist societies, organizations affiliated with the C.M.A. and other related groups, met in conjunction with the 94th Annual Meeting:

The Canadian Tuberculosis Association—Annual Business Meeting, Monday morning, June 19; Queen Elizabeth Hotel.

Quebec Anti-Tuberculosis Association — Annual Business Meeting, Monday afternoon, June 19; Queen Elizabeth Hotel.

Canadian Thoracic Society — Annual Scientific Meeting, Tuesday, June 20; Queen Elizabeth Hotel.

Canadian Rheumatism Association — Executive Committee Meeting, Sunday evening, June 18; Annual General and Scientific Meetings, Monday, June 19, and Tuesday, June 20; Queen Elizabeth Hotel.

Trans-Canada Medical Plans — Medical Directors Meeting, Wednesday, June 21, Queen Elizabeth Hotel: Commission Meeting, Thursday, June 22, and Saturday, June 24; Queen Elizabeth Hotel.

Canadian Medical Protective Association—Annual Meeting, Wednesday, June 21; Queen Elizabeth Hotel.

College of General Practice of Canada—Annual General Assembly—Montreal French and English Sub-Chapters, Thursday morning, June 22; Quebec Chapter, Thursday afternoon, June 22; Queen Elizabeth Hotel.

Canadian Society of Internal Medicine — Annual Business Meeting, Friday, June 23; Queen Elizabeth Hotel.

Montreal Interns and Residents—Panel Discussions on Postgraduate Medical Education and Specialty Training, Monday afternoon, June 19; Queen Elizabeth Hotel.

Canadian Association of Pathologists — Business Meeting, Thursday evening, June 22, Montreal Children's Hospital; Annual Scientific Meeting, Friday, June 23, and Saturday morning, June 24; Hôtel-Dieu Hospital, Montreal.
Annual Dinner, Friday, June 23, Redpath Hall, McGill University.

Montreal General Hospital Alumni—Reception, Dinner and Dance, Friday evening, June 23; Queen Elizabeth Hotel.
Ward rounds, operations, and tours of the hospital, Saturday, June 24; Montreal General Hospital.

Canadian Academy of Allergy — Annual Meeting, Sunday evening, June 18, through Tuesday, June 20; Mont Tremblant Lodge, Mont Tremblant, Quebec.

Registrars' Meeting—Sunday, June 18, Office of The College of Physicians and Surgeons of the Province of Quebec.

SCIENTIFIC EXHIBITS

The following exhibits illustrating a wide variety of phases of medical science were displayed on the Convention Floor of the hotel throughout the Annual Meeting:

Occupational Health (Information Services Division; Department of National Health and Welfare)—Designed to alert physicians to the incidence of occupational disease in Canada and to familiarize the profession with government facilities for prevention and diagnosis of such disorders.

The Sphinx of Diseases (Canadian Arthritis and Rheumatism Society: J. N. Swanson, M.D., Toronto)—A pictorial presentation of the objectives of the Society and the methods employed in their pursuit, including support of medical research, professional and public education, and the provision of physiotherapy, medical social work and related services to assist in the treatment of suffering from rheumatic disorders.

Differential Diagnosis of Arthritis (J. P. Gofton, M.D., Vancouver: The Canadian Rheumatism Association and The Canadian Arthritis and Rheumatism Society)—Radiological, clinical and laboratory features of common forms of arthritis in a three-panel display with the object of presenting the manifestations of importance in differentiation of the more frequently encountered types of joint disease. The information in this display was selected for its importance rather than as an encyclopedic representation of all manifestations of the diseases concerned.

Anticoagulants and Fibrinolysins (J. B. Armstrong, M.D., F.R.C.P.[C], Toronto: The Heart Foundation of Canada) — Demonstration of basic mechanisms of thrombus formation and blood coagulation and the effect of various drugs thereon; an outline of some tests of the coagulation process; a review of some problems of long-term anticoagulant therapy; and an illustration of the basic concepts of fibrinolysins and their current place in therapy.

The Parasites of Man in Canada (Prof. T. Cameron, Dr. Tanner and Dr. Donald M. Webster, McGill University)—Illustration of the more common parasites with more detailed information on the serology, pathology and epidemiology of trichinosis and echinococcosis, diseases of increasing importance in the north.

Thoracic Surgery in Pediatrics (P. P. Collins, M.D., J. C. Ducharme, M.D., and J. Doray, M.D., Ste. Justine Hospital, Montreal)—An exhibit outlining the scope of thoracic (excluding cardiovascular) surgery in pediatrics, under the headings of congenital anomalies, tumours, acute and chronic infections and reconstructive surgery of the esophagus.

Surgical Etiology of Acute Respiratory Diseases in the Newborn (J. C. Ducharme, M.D., and P. P. Collins, M.D., Ste. Justine Hospital, Montreal)—The importance of early diagnosis of atresia of the choanae and esophagus, tension pneumothorax, and diaphragmatic hernia; an outline of clinical features of these disorders; and methods of facilitating their diagnosis and emergency treatment.

Surgery of Coronary Artery Disease (H. P. Hill, M.D., and A. Vineberg, M.D., Montreal)—Experimental results and pathological studies of internal mammary artery implantation and Ivalon sponge procedure with a 5-9 year follow-up of human cases.

Treatment of Acquired Lesions Using Extracorporeal Circulation (A. Vineberg, M.D., M. McGregor, M.D., J. Palmer, M.D., and J. Gutelius, M.D., Montreal)—A review of three years' experience in treatment of 28 patients with mitral insufficiency, mitral stenosis, artrial masses and aortic lesions, using extracorporeal circulation.

Chemotherapy of Inoperable Cancer By Isolation and Pump Perfusion (E. Tabah, M.D., Montreal) — A review of patients with inoperable cancer, treated at Montreal Royal Victoria Hospital, with anticancer agents by means of the isolation-perfusion technique, including: demonstration of the technique and the drugs employed; illustration of methods of continuously monitoring leakage of the anticancer agent into the general circulation, and of factors that help to minimize leakage as well as reduce systemic toxic effects of the drugs employed.

Vectorcardiography (Y. Desrochers, M.D., and P. L. Campeau, M.D., Institute of Cardiology, Montreal)—Demonstration of the technique of vectorcardiography and its value in clinical practice, with comparison of the cardinal electrocardiographic syndromes and their vectorcardiographic counterparts. This technique is chiefly of value in differential diagnosis of right ventricular hypertrophy, incomplete right bundle branch block, and normal hearts. It is also helpful in diagnosis of infarction of the diaphragmatic wall of the myocardium. This exhibit also included a demonstration of vector loops in cases of ventricular hypertrophy and bundle branch block, after cardiac surgery.

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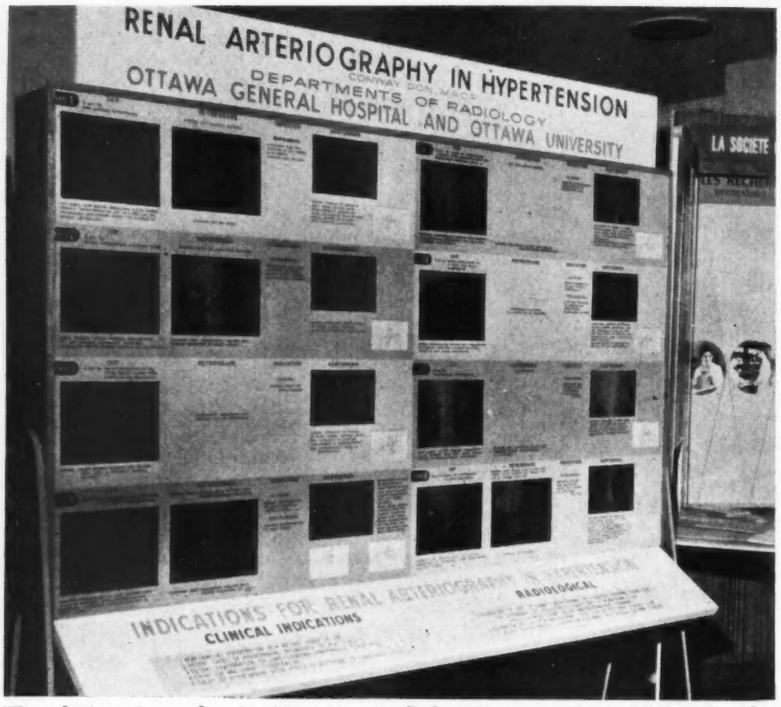


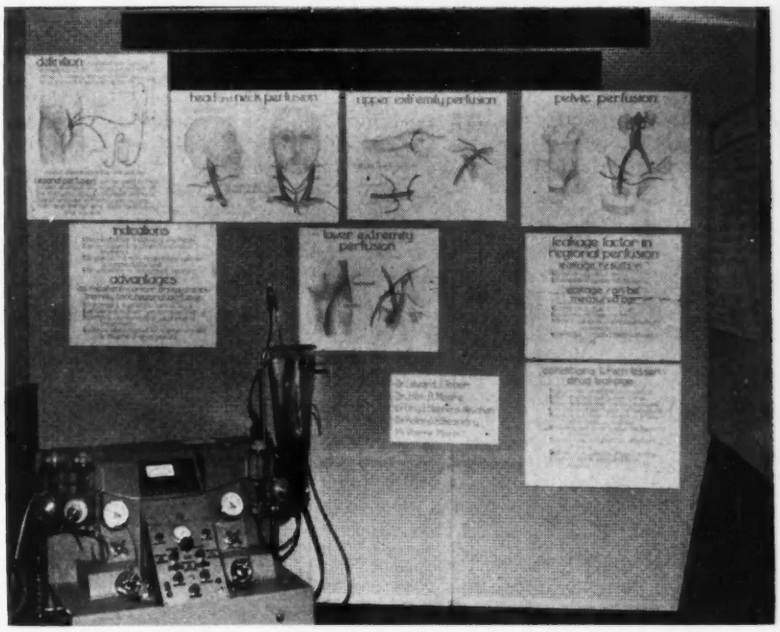
"Renal Arteriography in Hypertension" by Conway Don, M.R.C.P., the Departments of Radiology of the Ottawa General Hospital and the University of Ottawa.

"Differential Diagnosis of Arthritis", presented by Dr. J. P. Gofton, the Canadian Arthritis and Rheumatism Society and the Canadian Rheumatism Association.

"Cystic Fibrosis—Diagnosis and Treatment", by Dr. Donald A. Hillman of Montreal—an exhibit of the Canadian Cystic Fibrosis Foundation.

Preparation, Storage and Indications for Use of Human Bone Marrow (H. Baxter, M.D., and F. Inglis, M.D., Sub-Department of Plastic Surgery, Royal Victoria Hospital, Montreal)—Satisfactory procedures for obtaining autologous and homologous bone marrow have been developed. Fresh homologous marrow can be obtained without difficulty for infusion, but in certain diseases it is necessary to store autologous marrow for long periods before intravenous administration. Since current methods of storage result in rapid decrease in the number of viable cells after a few weeks, experiments are being conducted to determine if duration of survival of stored marrow can be enhanced. This exhibit illustrated the indications for the use of bone marrow infusions in human patients.

Malabsorption Syndrome (R. D. McKenna, M.D., Royal Victoria Hospital, I. T. Beck, M.D., and D. S. Kahn, M.D., Royal Victoria and St. Mary's Hospitals, Montreal)—A composite graph of the etiology, pathogenesis and clinical features of the different malabsorption syndromes, supplemented by typical histological patterns of peroral small bowel biopsies obtained in a variety of these diseases.



"The Chemotherapy of Inoperable Cancer by Isolation and Pump Perfusion", by Dr. Edward Tabah of Montreal.

Xylose Absorption Test (R. D. McKenna, M.D., Royal Victoria Hospital, I. T. Beck, M.D., and D. S. Kahn, M.D., Royal Victoria and St. Mary's Hospitals, Montreal)—The glucose tolerance test is unreliable as an index of carbohydrate absorption since glucose is actively metabolized in the body and its levels in the blood reflect processes in addition to absorption. The pentose, D+ xylose, being metabolized to a lesser extent, appears to be a useful material for testing carbohydrate absorption. Previously described methods for measuring blood xylose are laborious. This exhibit depicted a simplified technique for measuring blood xylose which could be carried out in the routine laboratory of any hospital and was found useful for screening patients suspected of having idiopathic sprue or other malabsorption syndromes.

A Study of the Pancreatic Ductal System (J. Greenhill, M.R.C.S., L.R.C.P., O. Retzer, M.D., and W. C. MacKenzie, M.D., University of Alberta Hospital, Edmonton)—Illustration of the variations of the pancreatic duct found in an unselected series of 130 postmortem examinations. Glands were studied by injection of radiopaque media or vinyl plastic. Photomicrographs of pathological changes such as squamous metaplasia, mucous gland hyperplasia and ductal proliferation were demonstrated.

Bone and Joint Transfer in Reconstruction (M. A. Entin, M.D., Royal Victoria Hospital, Montreal)—Demonstration of the various conditions in which autogenous bone and joint transfers are utilized in reconstruction, in patients with congenital or traumatic defects which interfered with normal function. Radiological changes of the transplanted bone and joints were recorded and correlated with clinical assessment of function after operation. Specific cases were demonstrated by diagrams and photographs.

The Fateful Months When Life Begins (National Institute of Neurological Disease and Blindness, and the Project Directors of 15 Collaborating Institutions, National Institutes of Health, Bethesda, Md., U.S.A.)—Demonstration of the research program and activities encompassing disorders of pregnancy, the birth process and many of the neurological deficits and disorders of early infancy currently being conducted at 15 medical institutions in the U.S.A. in collaboration with the National Institute of Neurological Diseases and Blindness, National Institutes of Health, Public Health Service, Department of Health, Education and Welfare, U.S.A. The exhibit included brief statements of the problem and relationships between factors and conditions affecting parents and the occurrence and course of abnormalities of their offspring, the purpose of the study and some of the etiological factors which may result in deficits and deviations at the outset of pregnancy. Sixteen colour transparencies illustrated the spectrum of clinical investigations including prenatal interviews and examinations, obstetrical procedures during labour and delivery, neurological examinations at birth and during the neonatal period, and studies in placental pathology.

Arterial Aneurysms (J. C. Luke, M.D., Royal Victoria Hospital, Montreal)—Illustrations in large colour transparencies of various types of arterial aneurysms and the operative procedures in resecting and grafting of an abdominal aortic aneurysm. Statistical data were presented on cases treated at the Royal Victoria Hospital, with arteriograms of the aneurysms demonstrated by contrast material.

Timing in Pediatric Surgery (H. E. Beardmore, M.D., G. M. Karn, M.D., H. F. Owen, M.D., and D. R. Murphy, M.D., Montreal Children's Hospital)—Demonstration of the optimum age at which some of the common surgical disorders of childhood should be corrected.

Evaluation of Bronchodilation with Intermittent Positive Pressure Breathing (M. Groszman, M.D., I. O. Berker, M.D., and D. Goltman, M.D., Mount Sinai Sanatorium, Ste. Agathe des Monts, Quebec)—A summary of findings in 24 patients with different cardiopulmonary diseases, depicted in figures and charts, stressing the subjective and objective effects of intermittent positive pressure breathing with a bronchodilator (Vaponefrin). Indications for and contraindications to this form of treatment were shown, together with illustrative chest radiographs and pulmonary function studies.

Cystic Fibrosis: Diagnosis and Treatment (D. A. Hillman, M.D., Montreal Children's Hospital; Canadian Cystic Fibrosis Foundation, Brantford, Ontario)—Illustration of the organs affected by cystic fibrosis, how sweat is obtained for diagnosis, and some of the drugs and therapy equipment used in treatment. A plastic model of a cutaway lung was used to depict the pulmonary damage caused by this disease.

Medical Lessons of The Past: Diagnosis and Treatment (History of the Medical Department, U.S. Army, in World War II: H. Van Cott and J. B. Coates, Jr., Colonel, M.C., U.S.A., Historical Unit U.S. Army Medical Service, Walter Reed Army Medical Center, Washington, D.C.)—A collection of medical volumes with clinical values as great as their historical interest.

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The U.S. Army Medical Service is now analyzing its enormous experience which has practical pertinence in the present atmosphere of world tension. In mass disaster, military or natural, many lives will be lost unless the medical profession capitalizes on the lessons learned in World War II concerning the care of large numbers of injured. Advance knowledge of such emergencies must be recognized before the event, in contrast to the lack of such information that resulted from inadequate publicity of the medical history of World War I when many medical lessons learned in that conflict were developed again in World War II at the expense of time, effort, limbs and sometimes lives.

Victorian Order of Nurses for Canada—Enlarged photographs showing various aspects of V.O.N. service were displayed on modern-design background screens. A nurse in V.O.N. uniform was in attendance to answer questions and to provide literature concerning the Order and its services.

Canadian Association for Retarded Children (Toronto)—A general descriptive display of the objectives, ideals and program of activities of the Retarded Children's movement in Canada.

College of General Practice of Canada (W. V. Johnston, M.D., Toronto, Executive Director)—An exhibit describing the College, its nature, its aims and goals; its past, present and planned contributions to the cause of the general practitioner.

Canadian Cancer Society (Montreal)- A display depicting the general outline of the cancer control program of the Canadian Cancer Society with special reference to public education and welfare facilities offered by the Society and a general outline of cancer research projects in Canada.

MEDICAL EXHIBITS

Through the co-operation of the Medical Exhibitors' Association of Canada, some ninety-one exhibits, including pharmaceutical, medical and surgical equipment, food products and medical books, were displayed throughout the annual meeting on the Convention Floor of the Queen Elizabeth Hotel. The exhibitors represented the leaders in their respective fields and their products symbolized developments in these fields in keeping with the scientific advancement of Canadian medicine.

MEDICAL FILMS

The showing of an impressive collection of some 28 medical films occupied a full three-day period on Tuesday, June 20, Wednesday, June 21 and Thursday, June 22.

The following films were included in the schedule: Hepatojugular Reflex; Disorders of Heartbeat; Heart Crippler; Evaluation of Hearing; Disinfection of Skin; Hospital Sepsis as a Communicable Disease; External Cardiac Massage; Prevention of Disability in Rheumatoid Arthritis (*The Canadian Arthritis and Rheumatism Society*); Disorders of Mobility; Gait and Musculo-Skeletal Disorders; The Menopause; Investigation of Human Sterility; Studies in Human Fertility; Surgical Treatment of Female Infertility; Cyto-Diagnosis of Uterine Cancer; Transportation of the Injured; Early Management of the Severely Burned Patient; Emergency Surgery of the Acutely Injured; Emergency Removal of Patients; Treatment of Pectus Excavatum (*Dr. Dafoe*); Anesthesia for Adenotonsillectomy (*Montreal Children's Hospital*); Acute Laryngo-Tracheobronchitis; Hernia in Infants and Children; Depression (*National Film Board*); Hostility (*National Film Board*); Feelings of Rejection (*National Film Board*); Over-Dependency (*National Film Board*); and The Psychiatric Hospital.

THE PHYSICIANS' ART SALON

The 1961 Physicians' Art Salon was exhibited on the Mezzanine Floor of the Queen Elizabeth Hotel from Tuesday, June 20, to Friday noon, June 23. Sponsored by Frank W. Horner Ltd. since its inception 17 years ago, the Art Salon has become a feature of increasing popularity at the annual meetings of the C.M.A. All paintings and photographs displayed were the creation of physicians or medical undergraduates from across Canada, each competing for awards in their various categories. The fine arts sections and the black-and-white photographs were on view from 9 a.m. to 9 p.m. daily. Prize-winning colour transparencies were shown twice daily in the Richelieu Room.

The three distinguished judges for this year's salon, Harold Beament, R.C.A., Albert Cloutier, R.C.A., and Geoff. F. Rogers, selected the following entries as award winners:

Traditional Fine Art

1st Prize, "Backyard"—J. G. Lister, M.D., Toronto, Ont.
2nd Prize, "Juniper Tree"—M. F. Newell, M.D., Edmonton, Alta.

Awards of Merit

"Harvest"—A. M. Linkletter, M.D., Pointe Claire, P.Q.
"Still Life"—Jean Lapierre, Montreal, P.Q.
"La Fin du Jour"—Pablo Tchang, M.D., Montreal, P.Q.
"Sun Flowers"—F. D. Locke, M.D., Lacombe, Alta.
"Nature Morte"—André D'Etchéverry, M.D., Sherbrooke, P.Q.

Contemporary Fine Art

1st Prize, "Heureuse Surprise"—J. M. Cordeau, M.D., Montreal, P.Q.
2nd Prize, "Composition No. 9"—T. J. Sullivan, M.D., Montreal, P.Q.

Awards of Merit

"Bichette"—Albert Jutras, M.D., Montreal, P.Q.
"Woman at the Well"—H. A. J. Schwarz, M.D., Edmonton, Alta.
"Snow in New York"—Jessie A. McGeachy, M.D., Saskatoon, Sask.

Portrait

1st Prize, "Dr. W. D. Duberger"—F. B. Bowman, M.D., Hamilton, Ont.
2nd Prize, "Artist"—Lionel Marks, M.D., Toronto, Ont.

Awards of Merit

"Dr. Harvey L. McNichol"—F. C. Emberton, M.D., Brooks, Alta.
"Tatooed Eskimo"—N. D. Abbey, M.D., Hay River, N.W.T.

Palette Club

"Green Door"—A. D. Pollock, M.D., Owen Sound, Ont.
"Beulah"—H. G. Ross, M.D., Montreal, P.Q.
"Portrait of Mafalda"—M. D. Charendoff, M.D., Toronto, Ont.

Monochromes

1st Prize, "Madeline"—Ronald I. Carr, Toronto, Ont.
2nd Prize, "Willy"—S. E. Slade, M.D., Squamish, B.C.
3rd Prize, "Between Classes"—Ronald I. Carr, Toronto, Ont.

Awards of Merit

"Patterns of Light"—B. Z. Steine, M.D., Montreal, P.Q.
"G"—F. C. Fraser, M.D., Montreal, P.Q.
"Deirdre"—J. Smith, M.D., Vancouver, B.C.
"Genevieve"—J. A. De Groot, Montreal, P.Q.
"White Tern"—R. W. Davidson, M.D., Victoria, B.C.

Colour Transparencies

1st Prize, "Look Out Below"—R. E. Hatfield, M.D., Calgary, Alta.
2nd Prize, "The Search"—J. P. Cordeau, M.D., Montreal, P.Q.
3rd Prize, "Ad Infinitum"—G. Brisebois, M.D., Montreal, P.Q.
4th Prize, "The Breaker"—Elizabeth MacKay, M.D., Toronto, Ont.

Awards of Merit

"Alert"—W. T. West, M.D., Brantford, Ont.
"Egypt, River Boat on the Nile"—F. Kalz, M.D., Montreal, P.Q.
"Riding High"—C. B. Hatfield, M.D., Calgary, Alta.
"On the Road to Mt. Zion"—L. Goldenberg, M.D., Toronto, Ont.
"School's Out"—J. G. Beatty, M.D., Edmonton, Alta.
"Debut"—G. Barrett, M.D., Nelson, B.C.
"Winter on Canadian Homestead"—F. H. Boone, M.D., Hamilton, Ont.
"The Cenotaph"—G. W. Hankins, M.D., Calgary, Alta.
"October Dawn"—J. D. Armstrong, M.D., Toronto, Ont.
"Flicker Family"—Bruce Charles, M.D., Toronto, Ont.
"Mad Sea"—R. Destroismaisons, M.D., Outremont, P.Q.
"Cathedral City"—Elizabeth MacKay, M.D., Toronto, Ont.
"Amaryllis Hybrid"—A. B. Jackson, M.D., Simcoe, Ont.
"Lynne"—Ronald I. Carr, Toronto, Ont.

GOLF TOURNAMENTS

Men's Tournament

The men's tournament was played at the Royal Montreal Golf Club on Thursday, June 22. Competition for the Ontario Trophy for the best individual gross score was apparently hotter than the weather, as the completion of 18 holes of play saw three contestants, Drs. M. M. Sereda of Edmonton and Y. Dion and T. P. Hale of Montreal locked in a dead heat. On the playoff hole Dr. Sereda repeated his triumph of last year, completing the competition with a winning low gross score of 78.

The Quebec Cup, awarded for the best individual net score for 18 holes, was won by Dr. L. Beaudoin of Montreal.

Ladies' Tournament

The ladies' tournament was held on Thursday, June 22, at the Mount Bruno Country Club, St. Bruno, Quebec. The winner of The T. Eaton Co. Trophy was Mrs. Malcolm D. Thorp of Sarnia, Ont. Mrs. George Maughan, Montreal, was runner-up.

[NOTE: The Scientific Program will be reported in a subsequent issue.—ED.]

PUBLIC HEALTH

SUMMARY OF REPORTED CASES OF NOTIFIABLE DISEASES IN CANADA*
ISSUED BY THE PUBLIC HEALTH SECTION, DOMINION BUREAU OF STATISTICS

Disease	Week ended (1961): April 29	May 6	May 13	May 20	Cumulative total since beginning of year: 1961	1960
Brucellosis (Undulant fever) (044)	4	4	7	4	46	27
Diarrhea of the newborn, epidemic (764)	2	4	—	10	43	20
Diphtheria (055)	—	—	—	2	35	12
Dysentery (045, 046, 048)	62	55	48	65	1,029	1,243
(a) Amebic (046)	—	—	—	—	4	1
(b) Bacillary (045)	40	20	34	28	528	1,110
(c) Other and unspecified (048)	22	35	14	37	497	132
Encephalitis, infectious (082.0)	—	—	—	—	—	—
Food poisoning: (049.0, 042.1, 049.2)	25	24	21	17	441	602
(a) Staphylococcus intoxication (049.0)	—	—	—	—	20	296
(b) Salmonella with food as vehicle of infection (042.1)	25	24	21	17	419	294
(c) Unspecified (049.2)	—	—	—	—	2	12
Hepatitis, infectious (including serum hepatitis) (092, N998.5)	170	170	181	161	4,478	2,504
Meningitis, viral or aseptic (080.2, 082.1)	1	7	1	1	57	73
(a) Due to poliovirus	—	—	—	—	3	23
(b) Due to Coxsackie virus	—	—	—	—	3	1
(c) Due to ECHO virus	—	—	—	—	—	1
(d) Other and unspecified	1	7	1	1	51	48
Meningococcal infections (057)	3	3	—	—	60	76
Pemphigus neonatorum (Impetigo of the newborn) (766)	5	—	—	—	6	5
Pertussis (Whooping cough) (056)	64	71	66	204	1,653	2,675
Poliomyelitis, paralytic (080.0, 080.1)	—	2	—	3	27	102
Scarlet fever and Streptococcal sore throat (050, 051)	265	230	254	296	7,091	13,575
Typhoid and Paratyphoid fever (040, 041)	6	7	3	5	94	144
Venereal diseases: (020-039)	365	305	347	304	6,834	6,372
(a) Gonorrhea (030-035)	326	266	300	259	5,991	5,638
(b) Syphilis (020-029)	39	39	47	45	842	741
(c) Other† (306-039)	—	—	—	—	1	3

*Figures for the Yukon are received four-weekly and are, therefore, shown in the cumulative totals only.
†Including chancroid, granuloma inguinale and lymphogranuloma venereum.

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BOOK REVIEWS

PROGRESS IN MEDICAL VIROLOGY. Edited by E. Berger and J. L. Melnick. 496 pp. Hafner Publishing Company, Inc., New York, 1961. $20.75.

Publication of the third volume of reviews by ten well-known investigators covering many aspects of medical virology of current interest will receive wide acclaim by virological investigators and university teachers. Schmidt and Lenette have reviewed comprehensively the methods involved and applications of serological techniques which are commonly employed in virus diagnosis. Their brief reference to fluorescent antibody procedures was amplified adequately by Poetschke's discussion of this valuable technique throughout the full range of readily isolated human viruses. Problems concerned with five possible modes of overwintering of Arborviruses in temperate zones were discussed critically by Reeves who personally has investigated this matter extensively. Gelfand's detailed account of the geographical distribution and methods of spread of the Coxsackie and ECHO viruses overlooked recent Canadian contributions such as the association of ECHO 19 and ECHO 20 viruses with aseptic meningitis. Results of numerous trials of living Sabin-type poliomyelitis vaccine which have been conducted in Russia and satellite republics have been crystallized by Smorodintsev through extensive use of tables. He has also discussed the remarkable tenfold reduction in incidence of mumps which was recorded as long as 18 to 21 months after subcutaneous injection of children at kindergartens with living mumps vaccine. Herrmann has described current procedures adopted in the search for and evaluation of antiviral drugs. Following a brief account of rubella in the first trimester, Blattner and Heys have presented an excellent review of fetal damage following maternal infection with varicella, herpes simplex, Coxsackie B and other viruses shortly before delivery. Dmochowski has provided a rich harvest of material, supported by excellent photomicrographs, describing the role of viruses in leukemia and polyoma.

The extensive bibliographies and clear tables have integrated many isolated pieces of information, thereby enhancing the value of this book to teachers, investigators and clinicians.

STRANGULATION OBSTRUCTION. American Lecture Series. Isidore Cohn, Jr. 273 pp. Illust. Charles C Thomas, Springfield, Ill., 1961. $11.75.

This is a well-written and well-published monograph. The author has certainly succeeded in establishing the importance of the entity, strangulation obstruction, apart from its lethal implications. The book contains an exhaustive review of all the ideas of the past which have been investigated to explain its symptoms, signs and course.

By far the greatest emphasis is placed on new ideas, and the experimental methods and means that have been employed to explain the morbidity and the mortality that accompany the disease. It is noted that dogs were used exclusively, and one can readily believe the assertion that no humans were ever better attended. The author does succeed in these experiments in establishing in this reader's mind that death, when it occurs in adequately treated strangulated bowel in dogs, is due to toxins produced by *Clostridium welchii*, associated with dead or dying tissue.

The series of 18 clinical cases illustrated do not convince the unbeliever that the Clostridium organisms are so consistently to blame for morbidity or mortality in humans. Surgeons who do frequent and routine swabs for culture at operation or during investigative procedures, do not doubt that Clostridium organisms are sometimes present. In humans, if an operation is inadequately or improperly performed, death may occur independently of bacterial invasion or antibiotic protection.

This book will undoubtedly serve as a classic reference for all who do experimental work in the search to solve the problems of pathological physiology in strangulation obstruction.

The abdominal or general surgeon who is not associated with an experimental laboratory will find many facts and ideas which will stimulate him to early diagnosis and prompt efficient treatment of the strangulated bowel.

MOLECULAR GENETICS AND HUMAN DISEASE. Edited by Lytt I. Gardner, 296 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1961. $12.75.

This volume is the outgrowth of a symposium held in April 1959, in which experts from many fields of genetics gathered to consider the relevance to medicine of the recent dramatic progress in understanding of gene structure and function. It was an illuminating and inspiring symposium, and even though much has happened in the intervening two years, the published record contains a great deal of interest to the physician. The book is stated by the publisher to bridge a gap between genetics and other health sciences, which presupposes some pre-existing knowledge of the fields at both ends of the bridge, and the physician will not find here an Everyman's guide to Mendelism. He *will* find able expositions of the current (1959) status of knowledge concerning the genetic code, genetic control of protein structure, and the relation of mutant genes to hereditary human diseases. The variety of topics covered can be judged by this partial list: the structure of DNA (Crick, Cambridge, of the Watson-Crick model); mutations and the control of protein structure (Ingram, M.I.T., discoverer of the relation of the sickle cell gene to a single amino-acid change in the globin molecule); the role of galactose-l-phosphate in the pathogenesis of galactosemia (Sidbury, Johns Hopkins); primaquine sensitivity (Kirkman, N.I.H.); recent advances in genetics of mice (Russell, Oak Ridge); sex chromosome aberration in man (Polani, Guy's Hospital); estimating consequences of an increased mutation rate (Newcombe, Chalk River). The final chapter is an excellent review of recent advances in human cytogenetics and contains references as recent as May 1960. Each presentation is followed by an edited version of the ensuing discussion by members of the audience. There is a useful glossary of the technical genetic terms used in the book.

(Continued on page 170)

THE PRESCRIPTION OF A NON STEROID

topical anti-inflammatory agent
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of effect, of cost.
Metanium is such a dermatological agent -
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(tannate, salicylate, oxide and peroxide) -
without steroid component.

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has been clinically elucidated
in a wide range of inflammatory conditions[1].

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describes an ingenious procedure
whereby
the anti-inflammatory effect of Metanium -
followed with the aid of intravenous
Coomassie Blue dye - was objectively determined,
and its properties defined specifically
as deriving from Ti ion.

Its place
in the therapeutic repertoire
is in those instances where it is felt
that steroid medications

may or must be withheld.

Metanium

****in contact and atopic dermatitis, infantile eczema, seborrhœic dermatitis** available as an ointment, in Transdermine base and as powder, with talc and kaolin** may be compounded, where an antibacterial effect is desired, with iodochlorhydroxyquinoline (2-3%), chloramphenicol (1%)** is compatible with most other traditional dermatological agents****

1 L. P. Ereaux: Canad. M.A.J.: 73, 31-34, 1955
2. F. Kalz and Z. Fekete: J. Invest. Derm.: January, 1961.

LEEMING MILES PHARMACEUTICALS INC., MONTREAL 28, QUEBEC

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(Continued from page 168)

CLINICAL OBSTETRICS AND GYNECOLOGY. Fetal Physiology and Distress, edited by Thaddeus L. Montgomery. Endocrinology, edited by Robert B. Greenblatt. 1144 pp. Illust. Paul B. Hoeber, Inc., New York, December 1960. Published quarterly. Subscription $18.00 a year.

The symposium on obstetrical anesthesia and analgesia covers the subject admirably. Those authors who approached their subject from basic principles provide the more stimulating papers in this section. The more practical, descriptive papers would appeal to the student rather than to the obstetrician or anesthetist.

The section on vaginal surgery has attempted to cover a vast subject in a rather small space. Perhaps descriptions of technique might better have been referred to than described and emphasis placed on the basic principles of vaginal surgery.

The inclusion of a paper on operations for double uterus and endometrial hyperplasia and a paper on vulvar operations seems incongruous.

The special article provides a stimulating discussion of a subject not commonly found in medical periodicals.

THE DEVELOPMENT OF THE INFANT AND YOUNG CHILD. Normal and Abnormal. R. S. Illingworth. 318 pp. Illust. E. & S. Livingstone Ltd., Edinburgh; The Macmillan Company of Canada Limited, Toronto, 1960. $4.70.

Is this child developing normally? Can these parents be assured that their fears and doubts are unnecessary? Is this child of normal growth and development for adoption?

These are a sampling of frequent problems in child care which make desirable more knowledge and a satisfactory source of reference regarding the development of the infant and child.

Such a reference is now available to the professions interested in this subject in this most readable and informative book by Dr. R. S. Illingworth.

In the opening chapters he has reviewed the literature and set forth his own numerous experiences and conclusions regarding ways of assessing the individual, and factors causing deviations in normal development.

The chapters on the examination of the newborn infant and child describe new observations and give the reader a renewed interest and excitement in the developmental examination which sometimes becomes a matter of dull routine.

In the final section, he demonstrates many observations which will save errors in judgment.

NEURAL MECHANISMS OF THE AUDITORY AND VESTIBULAR SYSTEMS. Edited by Grant L. Rasmussen and William F. Windle. 422 pp. Illust. Charles C Thomas, Springfield, Ill., 1960. $15.75.

This book represents proceedings of the tenth in a series of national conferences, called by the National Institute of Neurological Diseases and Blindness, in Bethesda, Md. These proceedings make available an exchange of knowledge between 32 scientists of international reputation who are engaging in current research in the field of the physiology of the ear and its neuromechanisms. Modern techniques and approaches are used to explore the basic mechanisms of hearing and equilibration. In view of the wide distribution of auditory defect in the population, such work has an immediate and important application.

Although the major emphasis of the program is on the physiology of the internal ear, the implications are much broader. In the cochlea there is an opportunity of studying the mechanism of excitation of sensory nerve endings. The vestibular system is closely related to the physiology of movement and posture and to their control. At the higher level, the studies deal with more complex mechanisms of auditory reception, interpretation and response. The studies here represented thus have a relationship to a much broader field of neuronal activity to various levels of complex neuronal integration.

This book would find a useful place in the library of those interested in otology and in neurophysiology, as well as for advanced students of neurology.

KRANZ MANUAL OF KINESIOLOGY. 4th ed. Clem W. Thompson, 159 pp. Illust. The C. V. Mosby Company, St. Louis, Mo., 1961. $3.75.

This little manual presents a well-illustrated review of the anatomy of muscles. It is designed largely for students in physical education, the detail being insufficient for students of medicine, for degree courses in nursing, or for physiotherapy and occupational therapy.

It can hardly, however, be called a manual of *kinesiology*, for it is concerned mainly with the prime movements of muscles, and gives little attention to such other important factors as decelleration, stabilization, fixation, and antagonistic action. For example, the importance of the deceleration activity of the vastus medialis and the tibialis anticus, both in normal and in running gaits, has not been mentioned. The anatomy of the small hand muscles, which, to the writer, seems so important in physical education and sports, has been sadly left out.

The laboratory and review exercises are quite worth while, and the chapter on "Analysis of Activities" would be of considerable interest to physical educators and athletic coaches.

OPTICS. An Introduction for Ophthalmologists. Kenneth N. Ogle. 265 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1961. $9.50.

The subject of optics always presents some difficulty to the ophthalmologist with a mediocre physico-mathematical background when first he pursues his ophthalmological career. It is therefore with considerable anticipation and interest that one approaches a new book on this subject.

The present volume is written by one of the outstanding authors on physiological optics and the book fully comes up to expectations. The subject is well presented and the mathematical concept well explained. There is a very welcome section on the principles of illumination which so often present difficulty to the practising ophthalmologist who is frequently consulted on this complex problem.

This reviewer's only criticism of the book is of the title. Surely it is not an "introduction" for ophthalmologists, as it sets out to be, but rather a book for the ophthalmologist who has already had a fair grounding in the practice of refraction with its theoretical background. The book will make a very valuable addition to every ophthalmologist's bookshelf and will be used frequently by the student and practitioner on a consultative basis.

(Continued on page 172)

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DOUBLE CATHETERIZING CYSTOSCOPE

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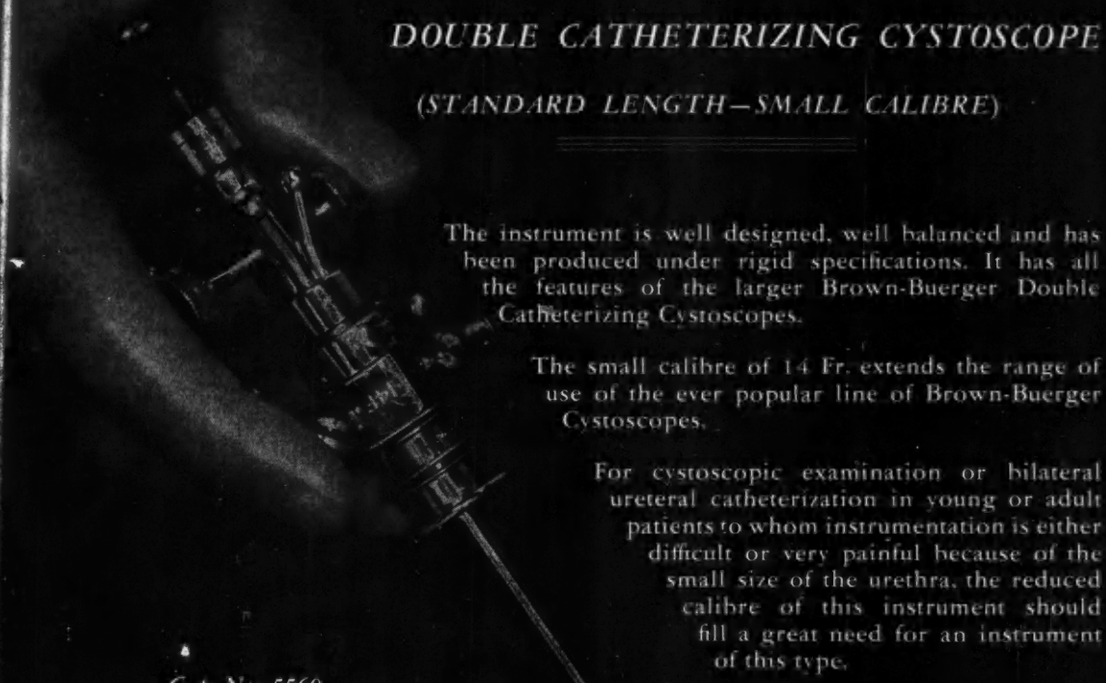

The instrument is well designed, well balanced and has been produced under rigid specifications. It has all the features of the larger Brown-Buerger Double Catheterizing Cystoscopes.

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For cystoscopic examination or bilateral ureteral catheterization in young or adult patients to whom instrumentation is either difficult or very painful because of the small size of the urethra, the reduced calibre of this instrument should fill a great need for an instrument of this type.

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There is a right angle examining telescope and a double catheterizing telescope.

The right angle examining telescope has a large clear field of 1¼" diameter and a 1" working distance.

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(Continued from page 170)

SEDAN'S RE-EDUCATIVE TREATMENT OF SUPPRESSION AMBLYOPIA. Being an Abridged English Version of Jean Sédan's Post Cure de L'Amblyope Rééduqué by T. Keith Lyle, Cynthia Douthwaite and Jill Wilkinson. 135 pp. Illust. E. & S. Livingstone Ltd., Edinburgh; The Macmillan Company of Canada Limited, Toronto, 1960. $4.25.

This book, which is an abridged English version of Jean Sedan's "Post cure de l'amblyope rééduqué", is a valuable addition to our material for dealing with cases of unilateral amblyopia.

The procedures advocated do not take the place of exercising the amblyopic eye with the fixing eye occluded in the young child, but are designed to maintain and improve the visual acuity achieved by this method, in the older child (over six years of age) and the young adult. The exercises may be done under the supervision of an ophthalmologist, or orthoptist in the clinic, or for home training.

The first section is devoted to proof-reading. Intentional errors in the text stimulate concentration and also provide an objective check on progress. The type ranges from large letters N48 to very small type N5.

There is a section containing arithmetical and pictorial problems with mistakes in the figures and differences between pictures. It also contains training exercises which help to improve visual orientation by the association of the eye and hand movements.

Perhaps the most important feature is that the book provides ideas for other exercises of a similar nature which can be used for home training.

CHILD GUIDANCE CENTRES. D. Buckle and S. Lebovici. Monograph Series No. 40. 133 pp. World Health Organization, Palais des Nations, Geneva, Switzerland, 1960. $4.00.

This is another admirable W.H.O. monograph. It is concerned with the development of child guidance centres, and discusses the uses and importance of such facilities in a sensible and practical manner.

In addition to presenting what can be considered an ideal organizational arrangement for a child guidance centre, a number of provocative questions are raised and discussed. For example, who should do psychotherapy? Should the basic training of a child psychiatrist be pediatric or psychiatric? Should child guidance centres be associated with pediatric hospitals? Is it always necessary for the director of a child guidance centre to be psychiatrist? Tacit recognition is given the fact that the number of child psychiatrists available now or in the foreseeable future cannot begin to meet the ever-increasing demands for service.

It is interesting to note that the monograph mentions a four-discipline team rather than the customary three. In addition to psychiatrist, psychologist and social worker, a fourth individual is distinguished—a psychiatrist, or a psychologist, who does psychotherapy.

Throughout the volume, reasonable and proper credit is given to the contribution which psychoanalytic thought has made to the development of child psychiatry, and vice versa. No mention is made, however, of the current interest in psychoanalytically based activity group therapy. Perhaps this is intentional.

The section on the formulation of diagnosis is of particular interest.

The institution and growth of child guidance centres is primarily an American development, beginning with Dr. William Healy in Chicago. The 1956 Lausanne Seminar, on which this monograph is based, was held under the auspices of the Regional Office for Europe of the W.H.O., but it seems unfortunate that no Americans were included among the participants. One would have thought that they might have had something to contribute.

Three of the appendices are worthy of note: a summary of Dr. Lebovici's ideas concerning the psychoanalytic concepts of the affective development of the child; a summary of the conclusions of the Seminar's Committee on Record-keeping; and a selected bibliography.

The volume meets the purpose for which it was intended. It will certainly be read with interest by those concerned with the establishment or organization of a child guidance centre.

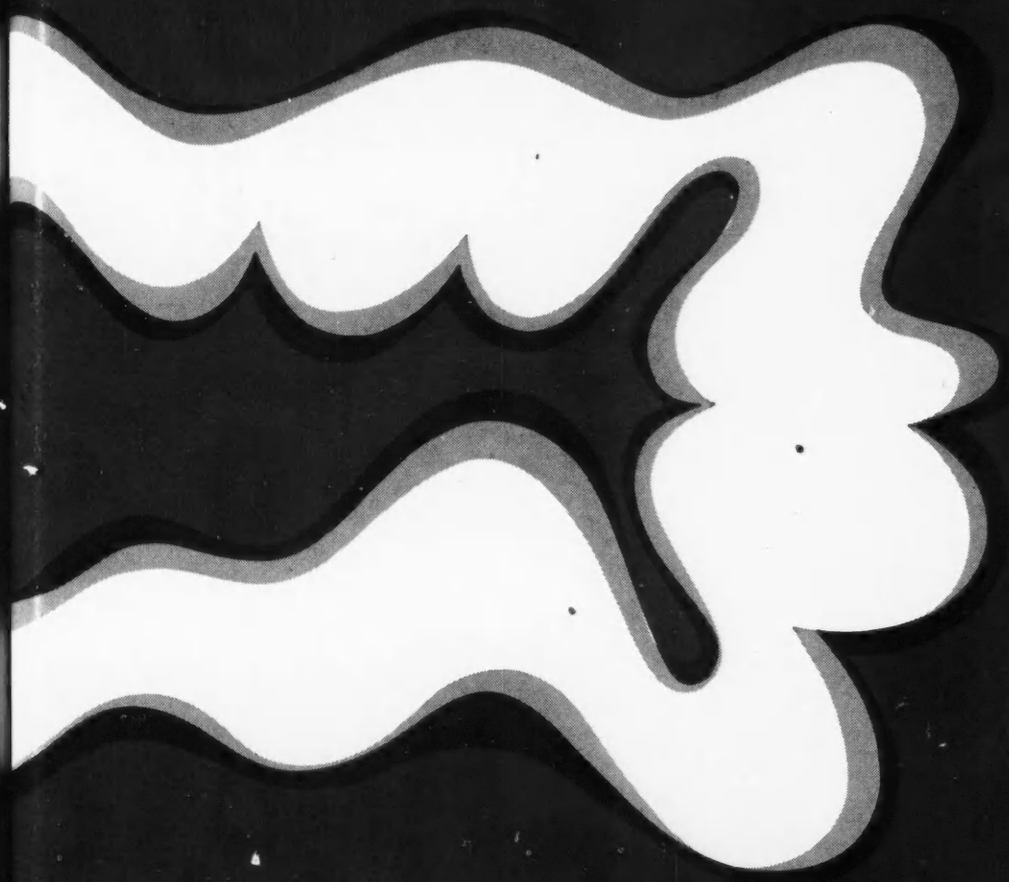
DIFFERENTIALDIAGNOSE INNERER KRANKHEITEN. Eine Kurzgefasste Darstellung für Aerzte und Studierende. Prof. Dr. Robert Hegglin. 913 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1960. $18.95.

The first edition of this textbook, which originated at the University of Zurich, appeared in 1952. That the seventh edition has been published within eight years attests to its popularity. Prefacing the first edition, Professor Hegglin justified his undertaking on the ground that the field of internal medicine is divided into so many subspecialties that an intimate knowledge of all is no longer possible. This book, written from the standpoint of the bedside clinician, is intended to facilitate orientation in these widely scattered areas.

The 554 illustrations are of high quality. They include reproductions of physical signs, x-ray films, fever charts, tables, and many excellent coloured photographs of typical skin manifestations (purpura, butterfly rash, spider nevi).

The introductory chapter on the technique and pitfalls of the art of differential diagnosis is followed by chapters on anemias, hemorrhagic diathesis, febrile states, headache, dyspnea, arrhythmias, cyanosis, hyper- and hypotensive states, lung shadows, hilar enlargement, and generalized lymphadenopathy; pain in the chest, abdomen, or extremities; diarrhea, constipation, icterus, splenomegaly, urinary abnormalities, edema, paralytic states, loss of consciousness and disturbances of electrolyte and acid-base balance.

This book contains a wealth of information. It undoubtedly has great merit for medical students, general practitioners, and internists, but there are certain drawbacks to its usefulness for readers of this continent: references are mainly to the European literature, and some key references to English writings are outdated. It would seem that dissemination of certain concepts in medicine is hampered by a language barrier. Although for the clinician it is refreshing to take cognizance of a different interpretation of observed facts, and perhaps of historical interest to read different names for well-known diseases or signs, this may confuse English-speaking medical students and thus detract from its value as a textbook for their use.



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Virtually non-toxic and free from side-effects

Convenience of two pharmaceutical forms:

- tablets — for overnight action
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Suppositories 10 mg. each: One suppository is usually sufficient to produce an action within ½ hour.

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MEDICAL NEWS *in Brief*

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FESTIVAL INTERNATIONAL PERMANENT DU FILM MEDICO-CHIRURGICAL ET SCIENTIFIQUE

L'ouverture de la 10e session du *Festival International Permanent du Film Médico-Chirurgical et Scientifique*, organisé en collaboration avec la *Gazette Médicale de France* par *l'Association Nationale des Médecins Cinéastes et des Cinéastes Scientifiques de France*, aura lieu à la Faculté de Médecine de Paris, en novembre 1961.

Les réalisateurs de films médico-chirurgicaux ou sciéntifiques de format 16mm substandard exclusivement, inédits en France, désirant participer à cette importante manifestation internationale, devront adresser leurs œuvres avant le *5 septembre prochain*, date de réunion du Conseil Technique chargé de la sélection des films inscrits.

Tous les envois doivent être effectués à l'adresse de *l'Association Nationale des Médecins Cinéastes et des Cinéastes Scientifiques de France*, 23, bld de Latour-Maubourg, Paris VIIe. Les participants étrangers ont intérêt à faire acheminer leur envoi par le canal de l'Attaché culturel de leur Ambassade à Paris, via leur Ministère des Affaires Etrangères.

Renseignements téléphoniques SOLférino 80-64.

THE NESTLE FELLOWSHIP

A fellowship of 10,000 new francs is awarded every year by the Nestlé Company, of France, to a physician who wishes to carry out special work in the field of nutrition.

The fellowship for 1962-1963 will be awarded in the spring of 1962. Candidates are requested to send the following to the International Children's Centre, Château de Longchamp, Bois de Boulogne, Paris XVI°:

(1) a *curriculum vitae* mentioning the work they have carried out on biological and social problems in feeding or nutrition of infants and children,

(2) a letter of introduction from one of their instructors,

(3) a description of the studies which they wish to pursue with the aid of the fellowship.

Candidates must have a sufficient command of the French language.

At the completion of their fellowship year the fellow or fellows will be expected to submit a scientific paper to the International Children's Centre on the subject which they studied during the year of their fellowship.

POPULATION CHANGES IN THE U.S.A.

Large cities in the northeastern and northcentral areas of the United States lost population in the last decade, while those in the south and west increased their number of residents by about one-fifth, it is reported by statisticians of the Metropolitan Life Insurance Company.

As a group, the largest cities—those with 250,000 or more residents in 1950—showed a population gain of only 4.4% between 1950 and 1960, compared with an increase of 18.5% for the country as a whole.

All eight large cities in the northeast lost population, the losses ranging from more than 10% in Boston and Pittsburgh to 1.4% in New York City. In the midwest, all cities with over 500,000 residents in 1950, except

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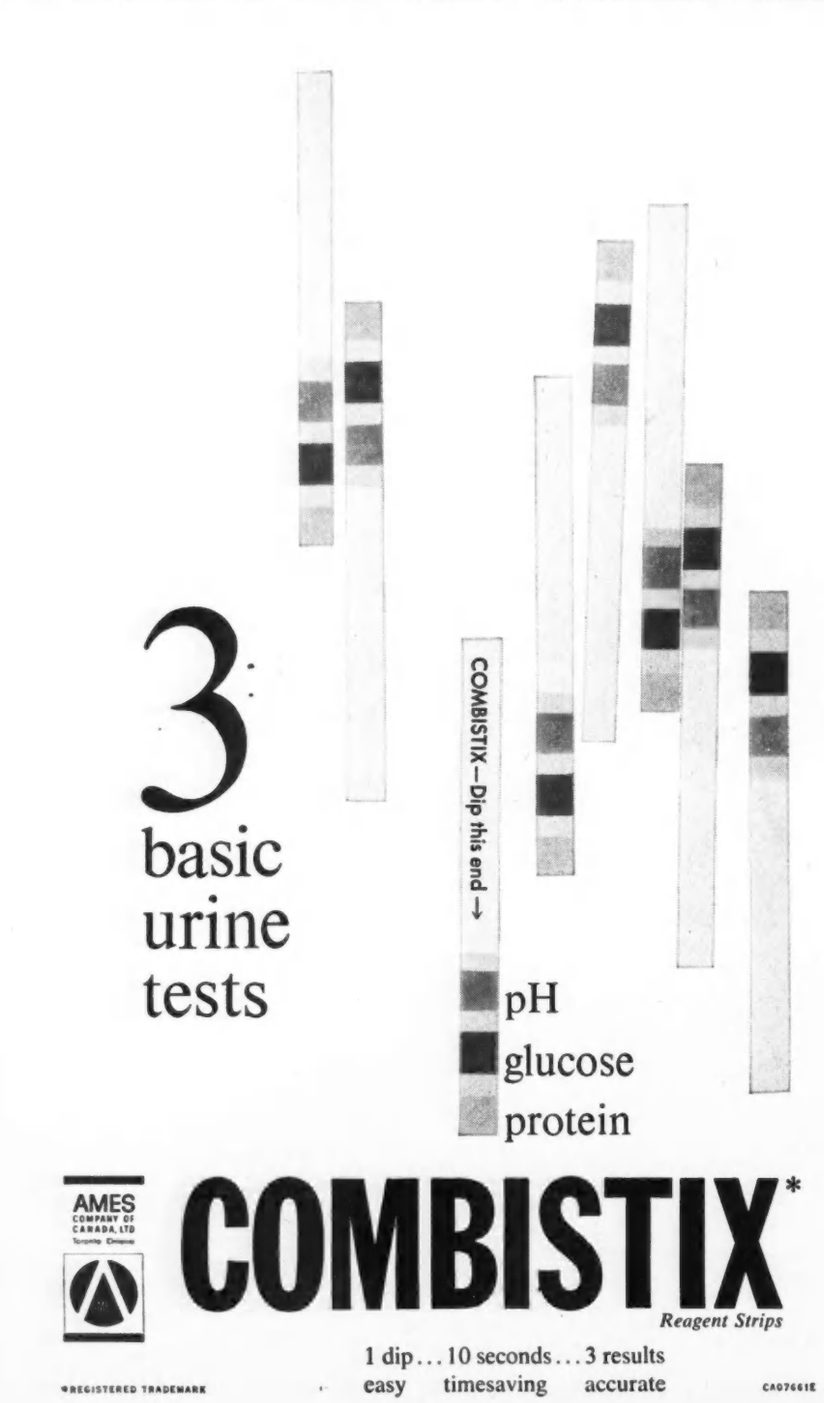
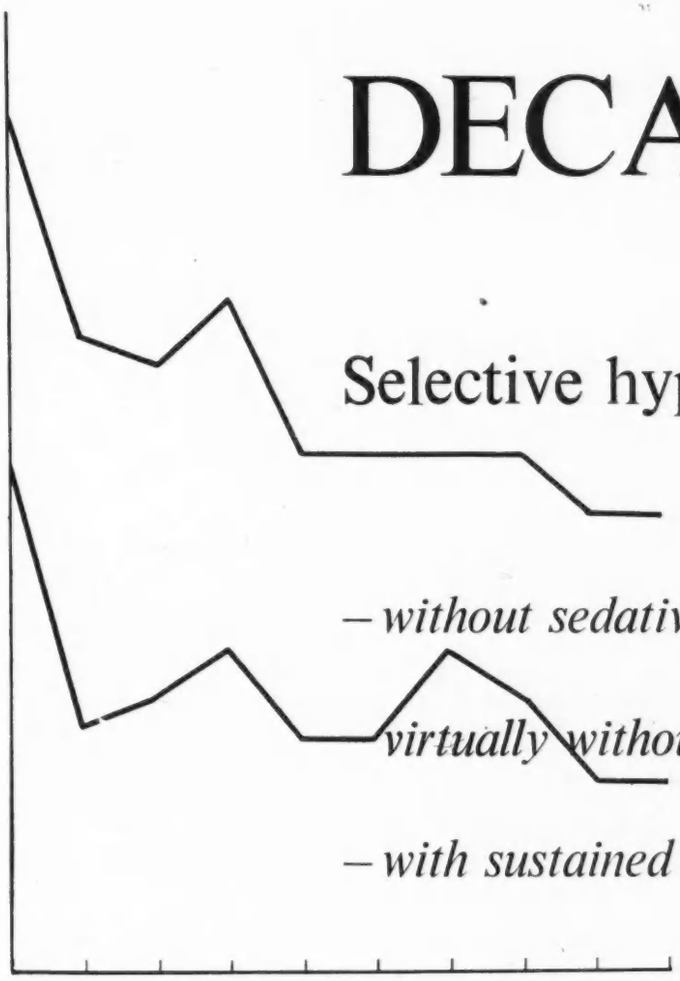


When mental alertness

must be retained...



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virtually without any side effects

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Packing: Scored tablets of 10 mg.
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MEDICAL NEWS *in brief*

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Milwaukee, lost population while those below that figure showed increases. In Milwaukee, as well as in Kansas City, Indianapolis and Omaha, all or most of the increase was due to the annexation of surrounding territory.

Most of the large cities in the south and west grew rapidly between 1950 and 1960. San Diego led all of the 41 large cities with a 71% increase, and five others—Houston, Dallas, San Antonio, Atlanta and Long Beach—recorded gains of at least 37%, or twice the national rate.

Los Angeles continued its vigorous growth, its population expanding by 25.8% to 2,479,015 in 1960. This is in sharp contrast to the other four cities with over 1,000,000 residents, each of which lost population. As a result, Los Angeles overtook Philadelphia and is now the nation's third largest city.

"Migration has been an important factor in the differential rates of growth within the United States," the Metropolitan statisticians point out. "In the north, for example, many families left the large cities for the suburbs or smaller cities. By contrast, in the south the large cities have tended to grow at the expense of the towns and rural areas. At the same time, California has attracted large numbers of people from other states. Most of the newcomers to the West have settled in the less-populated communities, as evidenced by the fact that the areas outside the large cities increased by 6.9 million, or 45%, during the 1950's."

BLOOD DONATIONS IN CANADA, 1960

A record high of 641,544 bottles of blood was collected by the Canadian Red Cross blood transfusion service in 1960. In turn, this blood provided transfusion therapy of whole blood and blood products for 234,886 patients in hospitals in every province. The Canadian Red Cross blood transfusion service is now one of the most outstanding throughout the world.

The Red Cross financial statement revealed that the cost of the blood transfusion service, $2,620,493, is the highest expenditure of the Society for the year and represented over 42% of the total expenditure for all Red Cross services. Based on a charge of $25 per bottle, which prevailed before the introduction of the blood transfusion service, the Red Cross estimates that the provision of whole blood and blood products saved patients in Canadian hospitals more than $16 million dollars in 1960. Red Cross laboratories also conducted 150,830 prenatal tests for the Rh factor. This is a free service for pregnant women and saved patients more than $750,000 last year. Since the inauguration of the Red Cross blood service in 1947, Canadians have donated 4,506,035 bottles of blood, and 1,810,288 patients have received one or more free transfusions.

In 1960, the Canadian Red Cross Blood Transfusion collected approximately 35.5 bottles per thousand population. During the same period in other countries comparable collections per thousand population by blood transfusion services operating on a voluntary donor basis were: United States, 13.6; Australia, 27.8; Great Britain, 22.0; and the Netherlands, 21.5.

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